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Early-onset preeclampsia, plasma microRNAs and endothelial cell function

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Condensation: Plasma microRNAs concentrations differ during preeclampsia as compared with healthy pregnancy. MiR-574-5p and miR-1972, which are both increased during preeclampsia as compared with healthy pregnancy, affect endothelial cell function *in vitro*.

Short version of title: Increased plasma microRNAs in early-onset preeclampsia affect endothelial cell function

AJOG at a glance:

A. Why was this study conducted?

We investigated if early-onset preeclampsia is characterized with different concentrations of plasma microRNAs as compared with healthy pregnancy and we studied *in vitro* if the microRNAs that were highly different between preeclampsia and healthy pregnancy might be involved in one of the main features of preeclampsia, endothelial dysfunction.

B: What are the key findings?

We demonstrated that concentrations of 26 plasma (precursor) microRNAs differed in concentration in early-onset preeclampsia as compared with healthy pregnancy. Furthermore, we showed that miR-574-5p and miR-1972, which showed increased plasma concentrations during preeclampsia as compared with healthy pregnancy, affect endothelial cell function *in vitro*.

C: What does the study add to what is already known?

Maternal endothelial cell dysfunction during preeclampsia is one of the underlying pathophysiological factors of one of the major signs of preeclampsia, hypertension. This study for the first time showed that 2 of the miRNA that were increased in preeclampsia vs. healthy pregnancy affected endothelial function *in vitro*, indicating that *in vivo* these miRNA may also contribute the

47 endothelial dysfunction in preeclampsia. The increased plasma microRNAs might be interesting

48 targets for reducing the endothelial dysfunction during preeclampsia.

ABSTRACT

Background: Preeclampsia is a hypertensive pregnancy disorder, in which generalized systemic inflammation and maternal endothelial dysfunction are involved in the pathophysiology. MiRNAs are small non-coding RNAs responsible for post-transcriptional regulation of gene expression and involved in many physiological processes. They mainly downregulate translation of their target genes.

Objective: We aimed to compare the plasma miRNA concentrations in preeclampsia, healthy pregnancy and non-pregnant women. Furthermore, we aimed to evaluate the effect of three highly increased plasma miRNAs in preeclampsia on endothelial cell function *in vitro*.

Study Design: We compared 3,391 (precursor) miRNA concentrations in plasma samples from early-onset preeclamptic women, gestational age matched healthy pregnant women and non-pregnant women using miRNA 3.1. arrays (Affymetrix) and validated our findings by real-time quantitative PCR (RT qPCR). Subsequently, endothelial cells (human umbilical vein endothelial cells) were transfected with microRNA mimics (we choose the three miRNAs with the highest fold change and lowest false discovery rate in preeclampsia vs. healthy pregnancy). After transfection, functional assays were performed to evaluate if overexpression of the microRNAs in endothelial cells affected endothelial cell function *in vitro.* Functional assays were the wound healing assay (which measures cell migration and proliferation), the proliferation assay and the tube formation assay (which assesses formation of endothelial cell tubes during the angiogenic process). To determine if the miRNAs are able to decrease gene expression of certain genes, RNA was isolated from transfected endothelial cells and gene expression (by measuring RNA expression) was evaluated by gene expression microarray (Genechip Human Gene 2.1 ST arrays [Life Technologies]). For the microarray we used pooled samples, but the differently expressed genes in the microarray were validated by RT qPCR in individual samples.

Results: No significant differences (fold change < -1.2 or > 1.2 with a false discovery rate < 0.05) were found in miRNA plasma concentrations between healthy pregnant and non-pregnant

women. The plasma concentrations of 26 (precursor) miRNAs were different between preeclampsia and healthy pregnancy. The 3 miRNAs which were increased with the highest fold change and lowest false discovery rate in preeclampsia vs. healthy pregnancy were miR-574-5p, miR-1972, and miR-4793-3p. Transfection of endothelial cells with these miRNAs in showed that miR-574-5p decreased ($p<0.05$) the wound healing capacity (i.e. decreased endothelial cell migration and/or proliferation) and tended ($p<0.1$) to decrease proliferation, miR-1972 decreased tube formation ($p<0.05$) and also tended ($p<0.1$) to decrease proliferation and miR-4793-3p tended ($p<0.1$) to decrease both the wound healing capacity and tube formation *in vitro*. Gene expression analysis of transfected endothelial cells revealed that miR-574-5p tended ($p<0.1$) to decrease the expression of the proliferation marker *MKI67.*

Conclusion: We conclude that in the early-onset preeclampsia group in our study different concentrations of plasma miRNAs are present as compared with healthy pregnancy. Our results suggest that miR-574-5p and miR-1972 decrease the proliferation (probably via decreasing MKI67) and/or migration as well as the tube formation capacity of endothelial cells. Therefore, these miRNAs may be anti-angiogenic factors affecting endothelial cells in preeclampsia.

Keywords: biomarker, endothelial dysfunction, endothelial cells, epigenetics, HUVEC, microarrays, microRNAs, miR-1972, miR-4793-3p, miR-574-5p, preeclampsia, proliferation, transfection, tube formation, systemic inflammation, wound healing

Introduction

Preeclampsia is a hypertensive pregnancy disorder affecting 2-8% of all pregnancies[2]. The poorly established[3] and/or perfused placenta[4] produces pro-inflammatory and anti-angiogenetic factors which are released into the maternal circulation[5–8]. These factors induce generalized systemic inflammation[9] and endothelial cell activation[10] and dysfunction[10,11], resulting in clinical signs of preeclampsia, such as hypertension and proteinuria[5,12].

MiRNAs are small (~22 nucleotides) non-coding RNAs responsible for post-transcriptional regulation of gene expression by targeting mRNAs for cleavage or inhibiting their translation[13]. MiRNAs play a critical role in many (patho)physiological cell processes, such as cell differentiation and proliferation[14,15]. In the circulation, miRNAs are often bound to proteins[16] or located inside microvesicles[17] which causes high stability of these small RNAs[18]. Circulating miRNAs serve as a communication system between cells[19] and circulating miRNAs may be involved in inflammation and endothelial function[20]. MiRNAs have been associated with many disorders, including atherosclerosis[21] and chronic kidney disease with proteinuria[22].

Other studies showed that the concentrations of certain miRNAs in the circulation before the onset of preeclampsia or during preeclampsia are different compared to healthy pregnant women[23–27]. Since miRNAs can target endothelial cells[19], we hypothesized that miRNAs which differ in concentrations during preeclampsia might contribute to maternal endothelial dysfunction. To examine this, (precursor) miRNA concentrations were measured in plasma samples of pregnant women with early-onset preeclampsia, healthy pregnant and non-pregnant women by microarray. Subsequently, endothelial cells were transfected with mimics of the miRNAs which were most highly elevated in preeclampsia vs. healthy pregnancy and endothelial cell function was evaluated by wound healing assay (to assess the effects of the miRNAs on endothelial cells migration and proliferation), cell proliferation assay and tube formation assays (to assess the effects of the miRNAs

120 on tube formation properties of endothelial cells) *in vitro*. Finally we investigated which genes were

121 affected by the miRNA mimics by microarray and real-time quantitative PCR.

122

Materials and Methods

For an extensive Materials and Methods please see the online Supplementary File.

Study design and rational

In the first part of this study, plasma miRNA concentrations of early-onset preeclamptic patients are compared with plasma microRNA concentrations of healthy pregnant and non-pregnant women. This was done by miRNA microarray technologies. Three miRNAs with the highest fold change (fold change > 1.8) and with a false discovery rate < 0.01 in preeclamptic as compared to healthy pregnant plasma were validated by real-time quantitative PCR. These three miRNAs were also selected for further investigation in the second part of the study.

In the second part of the study we examined the effects of increasing the concentrations of the selected miRNAs in endothelial cells. To increase miRNA concentrations in endothelial cells, endothelial cells were transfected with miRNA mimics (chemically modified RNAs that mimic endogenous miRNAs). Subsequently, assays were performed to assess endothelial cell function *in vitro*. These assays include a tube formation assay, a wound healing assay and a proliferation assay. The tube formation assay is a well-established model for measuring formation of endothelial cell tubes, which is part of the angiogenesis process *in vitro*[28]. The other two assays also assess processes that are important for angiogenesis[29]. The wound healing assay assesses migration/proliferation of cells after insertion of a linear scratch in the cell monolayer[30]. The proliferation assay measures proliferation of the cells, by measuring metabolic activity of the transfected cells over time.

Since miRNAs functions by decreasing mRNA expression, in the last part of this study it was investigated if the miRNAs were able to indeed modify gene expression pattern in the transfected endothelial cells. To do so, mRNA expression of the endothelial cells was characterized by gene expression microarray and validated by real-time quantitative PCR.

148

149 **Patient recruitment and plasma collection**

150 We included healthy non-pregnant women (n=10), healthy pregnant women (n=10) and
151 women diagnosed with early-onset preeclampsia (PE, n=10). The sample size of 10 subjects in each
152 group was decided using power calculations described in the article of Liu et al[31]. Preeclampsia was
153 defined according to the definition from the Practice Bulletin #203 "Chronic Hypertension in
154 Pregnancy": a systolic blood pressure of ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg on
155 two or more occasions at least 4 h apart after 20 weeks of gestation in women with a previously
156 normal blood pressure, and proteinuria ≥ 300 mg/24 h[32]. Samples included in this study were from
157 early-onset preeclampsia, these women all delivered before week 34 of gestation and did no show
158 comorbidities, such as autoimmune diseases (i.e. diabetes, antiphospholipid syndrome, SLE) or
159 chronic hypertension. Healthy pregnant women and PE were matched for gestational age at
160 sampling. The medical ethical committee of the UMCG approved this study, and informed consent
161 was signed by all participants.

162

163 **MicroRNA array**

164 Total RNA was isolated from the plasma samples and 1 µg was labeled and hybridized to
165 miRNA 3.1 arrays targeting 3,391 human (precursor) microRNAs ((pre-)miRNAs) (P/N 90215,
166 Affymetrix). The miRNAs targeted by this array were all (precursor) miRNAs known at that moment
167 (100% miRBase v17 coverage).

168

169 **MicroRNA array quality control and data analysis**

170 Please see the online Supplementary File. The miRNAs with the highest fold change (fold
171 change > 1.8) and with a false discovery rate < 0.01 in PE vs. healthy pregnant were chosen (miR-574-
172 5p, miR-1972 and miR-4793-3p) for further analysis.

173

MicroRNA array validation by real-time quantitative PCR

Validation of the array was done by real-time quantitative PCR (RT qPCR) using miRNAs which were found to change with the highest fold change and with a false discovery rate < 0.01 in preeclampsia vs. healthy pregnancy (miR-574-5p, miR-1972 and miR-4793-3p). cDNA was prepared and RT qPCR was performed on a StepOnePlus™ Real-Time PCR System machine (Applied Biosystems). Relative expression levels were calculated by the $2^{-\Delta CT}$ method and normalized against expression levels of the relatively stable endogenous control hsa-miR-191-5p.

Human umbilical vein endothelial cell culturing

Isolation of human umbilical vein endothelial cells was performed in the endothelial cell facility of the UMCG using umbilical veins from term pregnancies without complications (such as autoimmune diseases, preeclampsia and intra uterine growth restriction) and cells were pooled from at least 2 donors and cultured as described before[33]. Please see the online Supplementary File for further details.

Transfection of endothelial cells with miRNA mimics

50% confluent endothelial cells (passage 3) were transfected with *mir*Vana miRNA mimics (miR-574-5p, miR-1972 or miR-4793-3p) or the *mir*Vana miRNA mimic negative control #1 (Ambion). Please see the online Supplementary File for further details.

Tube formation assay

The tube formation assay is a well-established model for measuring tube formation, i.e. the ability of the endothelial cells to form capillary-like structures *in vitro*. This is part of the angiogenic process[28]. Matrigel basement membrane matrix (Corning) was pipetted into the inner wells of the µ-Slide Angiogenesis (Ibidi). Slides were incubated for 45 min at 37°C. The transfected endothelial cells were collected after 48 h of incubation and 10,000 endothelial cells were seeded into each well on

top of the matrigel. After 12h at 37°C, pictures were taken. Tube formation was quantified as total amount of loops (i.e. numbers of capillaries formed), total tube length (length of the capillaries) and total branching points (number of interconnections between the tubules, which gives information on how endothelial cells organize themselves) by using Wimasis, 2017 (n=5). (WimTube: Tube Formation Assay Image Analysis Solution. Release 4.0. Available from: https://www.wimasis.com/en/products/13/WimTube).

Wound healing assay

Endothelial cell migration and/or proliferation potential was assessed by the wound healing assay of the transfected endothelial cells. A linear scratch was made using a sterile pipet tip. Pictures were taken of the same area of the scratch after 0, 4, 8, 12, and 24 h of incubation at 37°C. To measure how long it takes to close the wound, the surface area of the scratch was measured using ImageJ (n=5).

WST-1 assay for cell proliferation

Since the wound healing assay evaluates both migration and proliferation, but does not allow discrimination between these processes, we also performed a proliferation assay, which specifically measures proliferation of the cells. To do so, the metabolic activity of transfected endothelial cells was measured by colorimetric WST-1 assays (4-[3-(4-Iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate) (cat. no. 05015944001; Roche Applied Science). 48 hours after transfection, 10 µl WST-1 solution was added to culture medium in all wells and incubated for 2h at 37°C. Subsequently, absorbance was measured at 450 and 750 (background) nm. The WST-1 assay measures the number of viable cells. An increase in the number of viable cells indicates proliferation, a decrease of the number of viable cells indicates cell death (n=5).

Gene expression microarray of transfected endothelial cells

To identify miRNAs targets in endothelial cells, total RNA was isolated from transfected endothelial cells and gene expression was evaluated by microarray.

Gene expression microarray was performed with pooled samples from 6 independent experiments. Four pooled samples were tested: endothelial cells transfected with the control miRNA and endothelial cells transfected with the miR-574-5p, miR-1972 or miR-4793-3p mimics. Total RNA (100 ng) was labeled and hybridized to whole genome Genechip Human Gene 2.1 ST arrays coding 25.088 genes and transcripts (Life Technologies, the Netherlands). For microarray quality control and data analysis please see the online Supplementary File.

RT qPCR of potential miRNA targets

To confirm the potential targets of the miRNAs identified by microarray, RT qPCR was used. Total RNA was reverse transcribed and RT qPCR was performed on a StepOnePlus™ Real-Time PCR System machine (Applied Biosystems). Relative expression levels were calculated by the $2^{-\Delta CT}$ method and normalized against expression levels of *36B4*.

Statistics

Please see the online Supplementary File.

Results

Patient characteristics

All PE patients included were diagnosed with early-onset preeclampsia, i.e. they all delivered before 34 weeks of gestation. Since blood sampling of healthy pregnant women was matched for gestational age with the PE group, there were no differences in gestational age at sampling. There were also no differences in maternal age, parity and smoking between the pregnant groups (Table 1). However, the PE patients delivered earlier and the newborns weighed less compared to the healthy pregnant group (Table 1). The non-pregnant women did not differ in age or smoking from the pregnant groups (Table 1).

Differences in microRNA concentrations

No precursor (pre) miRNAs were significantly (fold change < -1.2 or > 1.2 with a false discovery rate < 0.05) increased in healthy pregnant compared to non-pregnant women. In PE, 26 (pre-)miRNAs were detected in different concentrations compared to healthy pregnant women, which included an increase in concentrations of six precursor miRNAs and 19 miRNAs and the decrease in concentrations of one miRNA (Table 2).

Validation of the three mostly increased microRNAs in PE by RT qPCR

As a microarray may give false positive, we validated the array data with RT qPCR. Expression levels of the three miRNAs with the highest increase in concentrations (and a false discovery rate < 0.01) in PE vs. healthy pregnant women (miR-574-5p, miR-1972, miR-4793-3p) were evaluated. For all three miRNAs, a significant linear correlation was found between array and RT qPCR data (Fig. 1A-C). Concentrations of miR-574-5p (Fig. 1D) and miR-1972 (Fig. 1E) were increased compared to both healthy pregnancy and non-pregnant women. The miR-4793-3p concentrations were increased in both PE and non-pregnant compared to healthy pregnant women (Fig. 1F).

MiR-1972 attenuates tube formation *in vitro*

Endothelial cells were transfected with miRNA mimics to examine if the miRNAs, with the biggest change in preeclampsia vs. healthy pregnancy, affected endothelial cell function. Endothelial cell function was assessed by the tube formation assay (Fig. 2), which assesses the capability of the endothelial cells to form capillary-like structures. All transfected endothelial cells were able to form tubes (Fig. 2A). Transfection with miR-1972 significantly ($p = 0.049$) reduced the amount of loops formed as compared with the control. Transfection with miR-4793-3p tended ($p = 0.068$) to reduce the amount of loops formed as compared with the control, while miR-574-5p did not affect loop formation (Fig. 2B). No differences were detected in total tube length between the groups (Fig. 2C). The total branching points were significantly reduced after miR-1972 transfection as compared with control ($p = 0.029$) and tended to be reduced after miR-4793-3p transfection as compared with control ($p = 0.085$), while miR-574-5 did not affect the total branching points (Fig. 2D)

MiR-574-5p negatively affects wound healing *in vitro*

The wound healing assay was used to assess migration and/or proliferation of the endothelial cells. Therefore, a scratch was made in the wells with transfected endothelial cells and pictures were taken after 0, 4, 8, 12 and 24 h (Fig. 3A) to evaluate wound healing. Wound healing was quantified by measuring the percentage of wound closure in time (Fig. 3B). The area under the curve revealed that miR-574-5p overexpression in endothelial cells significantly reduced wound closure as compared with control ($p = 0.031$), while miR-4793-3p overexpression tended to reduce wound closure as compared with the control ($p = 0.062$)(Fig. 3C). MiR-1972 did not influence wound closure.

MiR-574-5p and miR-4793-3p tend to decrease proliferation of endothelial cells *in vitro*

To further examine which factor, decreased proliferation or migration, was responsible for the reduced wound healing capacity after miR-574-5p transfection, a proliferation assay was performed. It appeared that miR-574-5p ($p = 0.063$) and miR-1927 ($p = 0.063$) tended to reduce proliferation of endothelial cells as compared with control endothelial cells, while miR-4793-3p did not affect proliferation in endothelial cells (Fig. 4).

MiR-574-5p suppresses the proliferation marker *MKI67*

To investigate which genes in endothelial cells are regulated by the three miRNAs, gene expression of transfected endothelial cells was evaluated by gene expression array and validated by RT qPCR. Array data of pooled samples of miR-574-5p transfected endothelial cells showed potential silencing (a decreased expression > 50%) of 1,034 genes (Supplementary Table 3). *SLC31A1* was downregulated with the highest fold change (fold change = -12.95) and thus this gene was chosen for validation with RT qPCR in all samples. *MKI67* (fold change = -1.51) was also chosen for validation with RT qPCR since *MKI67* is a marker for cell proliferation. For validation, samples were not pooled, but individual samples were used. RT qPCR validated that miR-574-5p overexpression (n=5) significantly decreased the expression of *SLC31A1* ($p = 0.031$) and tended to decrease the expression of *MKI67* ($p = 0.094$) as compared with control endothelial cells (n=5) (Fig. 5). The pooled array data of miR-1972 (Supplementary Table 4) and miR-4793-3p (Supplementary Table 5) showed potential silencing of 812 and 840 genes, respectively. The mostly downregulated genes in both cases were *RSAD2* (fold change miR-1972 = -8.33 and fold change miR-4792-3p = -10.20) and *CXCL10* (fold change miR-1972 = -7.94 and fold change miR-4792-3p = -6.69). We validated these genes with RT qPCR on the individual samples. This RT qPCR revealed, however, that these were not significantly decreased as compared with the control sample (data not shown). The genes encoding ICAM-1, VCAM-1 or other pro-inflammatory factors were not altered in expression. It seems therefore that these miRNAs do not affect endothelial cell activation and we decided not to focus on genes involved in endothelial cell activation.

Comment

Principal findings

In this study we identified (pre-)miRNAs with different plasma concentrations in early-onset preeclamptic women as compared with healthy pregnant women. We demonstrated that preeclampsia is characterized by changes in plasma levels of 26 (pre-)miRNAs as compared with healthy pregnancy. Subsequently, we studied the influence of the three miRNAs which were increased with the highest fold change (and a false discovery rate < 0.01) in preeclampsia vs. healthy pregnancy on angiogenic function of endothelial cells. This was done by transfecting endothelial cells with miRNA mimics of these miRNAs followed by assays evaluating processes involved in angiogenesis, i.e. the a wound healing assay, a proliferation assay and a tube formation assay. We showed that miR-574-5p negatively affected wound healing and tended to reduce proliferation of endothelial cells *in vitro*. MiR-1972 negatively affected tube formation and also tended to reduce proliferation of endothelial cells *in vitro*. MiR-4793-3p tended to decrease tube formation and tended to negatively affect wound healing. Thus, the early-onset preeclampsia group in our study is characterized with differences in plasma miRNA concentrations as compared to healthy pregnancy. We demonstrated that increased miR-574-5p and miR-1972 showed anti-angiogenic affects.

Comparison with existing literature

Our study revealed differences in plasma levels of miRNAs in early-onset preeclamptic vs. healthy pregnant women, which is in line with various previous studies[23–27]. Details about these studies are presented in Table 3. We found that the concentrations of 26 (pre-)miRNAs were different in preeclampsia vs. healthy pregnancy, the miRNAs which were mostly increased in concentrations being miR-1972, miR-574-5p and miR-4793-3p. However, our study differs from other studies: For example, miR-1972 and miR-4793-3p were not mentioned in any of the other studies evaluating miRNA expression in preeclampsia vs. healthy pregnancy and which also performed

genome-wide miRNA profiling[23,25–27]. Differences between studies might be explained by differences in sample collection (serum instead of plasma)[26,34], inclusion of early- or late-onset preeclampsia[23,24,26], gestational age at sampling[25,26], profiling methods[25] and/or ethnicity of patients[34,35]. MiR-574-5p, which was increased in PE in our study, was also found to be increased during or before preeclampsia in two other studies[23,24]. The fact that we are the third study to link this specific miRNA with preeclampsia, may indicate an important role of miR-574-5p in the development and/or the pathogenesis of preeclampsia. There are several miRNAs predominantly expressed in the placenta, including miRNAs located at the chromosome 19 microRNA cluster (C19MC), C14MC and the miR-371-3 cluster[36]. The 26 (pre-)miRNAs did not include any members of the C19MC, C14MC or the miR-371-3 cluster. This does not automatically imply that the placenta was not the source of the miRNAs. However, the miRNA could also arise from other sources, such as activated immune cells or maybe even activated endothelial cells themselves.

Overexpression of miR-574-5p in preeclampsia

We found that overexpression of miR-574-5p in endothelial cells resulted in a decreased endothelial wound healing capacity, i.e. a decreased capacity of migration and/or proliferation of endothelial cells. The strength of the wound healing assay is that it actively measures cell activity *in vitro*. However, the specific factors involved (migration or proliferation) cannot be addressed. In our study, the decreased wound healing capacity is probably (partly) induced by decreased proliferation since subsequent experiments revealed that miR-574-5p overexpression tended to inhibit proliferation of endothelial cells *in vitro*. Inhibited migration of endothelial cells probably also plays an important role. Furthermore, we also found that miR-574-5p overexpression tended to decrease the expression of *MKI67*, which encodes the well-known proliferation marker Ki-67[37]. Our data of the effect of miR-574-5p on proliferation are in accordance with two other studies[38,39]. MiR-574-5p overexpression in our study significantly reduced the expression of *SLC31A1*. This gene encodes for a high affinity copper transporter in the cell membrane. Copper transport is essential for cell function,

including proliferation[40]. The decreased expression of *SLC31A1* in our study might contribute to decreased proliferation of endothelial cells after miR-574-5p overexpression by limiting copper entry into the cells. Since both endothelial cell migration and proliferation are processes involved in angiogenesis[29], this miR-574-5p has anti-angiogenic properties, and this miRNA may contribute to the anti-angiogenic environment in preeclampsia.

Overexpression of miR-1972 in preeclampsia

Overexpression of miR-1972 in endothelial cells resulted in attenuated tube formation and tended to reduce proliferation. The tube formation assay is a well-established *in vitro* model for formation of endothelial cell tubes, a process important in the angiogenic process[28]. Preeclampsia is characterized with increased levels of circulating anti-angiogenic factors like soluble fms-like tyrosine kinase 1 (sFlt-1)[5] and soluble endoglin (sEng)[41]. Our data show that miR-1972, like miR574-5p, may also contribute to the anti-angiogenic environment in preeclampsia. However, as compared with miR574-5p, miR1972 seems to affect a different part of the angiogenic process, i.e. endothelial cell tube formation. Another study showed that overexpression of miR-1972 in chronic myelogenous leukemia cells inhibited cell division[42]. This might be in line with our results, since miR-1972 overexpression also tended to reduce endothelial cell proliferation. Since to our knowledge no previous research mentioned miR-1972 in relation with preeclampsia, further research is necessary to determine the exact role of miR-1972 during preeclampsia.

Overexpression of miR-4793-3p in preeclampsia

The third miRNA, which was increased during preeclampsia vs. healthy pregnancy was miR-4793-3p. Previous studies showed that miR-4793-3p concentrations were increased in un-ruptured cerebral aneurysm tissues[43] and decreased in the circulation during chronic thromboembolic pulmonary hypertension[44]. However, on a functional level not much is known about this particular microRNA. In our study, miR-4793-3p overexpression in endothelial cells tended to reduce tube

formation and tended to negatively affect wound healing *in vitro*, suggesting that this miRNA may potentially reduce angiogenesis in preeclampsia

Strengths and limitations

We extended our observational study on plasma miRNAs in preeclampsia with a mechanistic study in which we pinpointed the effects of the increased plasma miRNAs in preeclampsia on endothelial cell function *in vitro*. Using various techniques, we demonstrated that preeclampsia-specific miRNAs affected endothelial cell function, especially angiogenic function, *in vitro*. We note that the *in vivo* miRNA uptake mechanically differs from the *in vitro* transfection method used in this study. However, the transfection method, we used, is generally accepted[45–47] to enable investigating the effect of increased concentrations of specific miRNAs on cells. Moreover, the observed cellular effects are biologically plausible in the context of preeclampsia. Although we included non-pregnant, pregnant and preeclamptic patients, our study was a relatively small study, with 10 individuals in each group. However, we included a relatively homogeneous group of preeclamptic women, which were all early onset and gestational age at sampling was perfectly matched with healthy pregnant women.

Clinical implications

The miRNAs which differed in concentrations during preeclampsia maybe modulators of endothelial function in preeclampsia. Our findings fit into the current understanding of the pathophysiology of preeclampsia. The poorly established placenta in early-onset preeclampsia produces many proinflammatory[8] and anti-angiogenic factors (which may include the miRNAs found in our study)[5,7] into the maternal circulation inducing generalized systemic inflammation[9] and endothelial cell activation and dysfunction[10,11]. If the inflammatory cells or endothelial cells also produce the miRNAs identified in our study, then these miRNA may also target the endothelial cells, with anti-angiogenic effects.

If these microRNAs are already present early in pregnancy, these microRNAs may contribute to a better biomarker profile for early preeclampsia diagnostics. Existing circulating biomarkers profiles (including placental growth factor, sFlt-1 and sEng) are at the moment still limited for prediction of preeclampsia[48] and would therefore benefit with additional early biomarkers.

The miRNAs might also be interesting future targets for reducing endothelial dysfunction during preeclampsia. Endogenous miRNAs can for example be inhibited using synthetic antisense microRNAs which are complimentary to the endogenous miRNA[49]. At this moment the possibilities of such microRNA therapeutics are under extensive investigation and a small number of microRNA therapeutics are already at the stage of clinical trials[49,50].

Research implications

Future research should demonstrate if the effects of the miRNAs on endothelial cell function *in vitro* also take place *in vivo*. This could first be tested in animal experiments, in which the effects of overexpression of the miRNA in animals could be tested. For example, transgenic mice could be developed to overexpress the miRNA of interest by incorporating a transgene[51]. To investigate the effect of the miRNA specifically in the endothelium, expression of the transgene could be made tissue specific (e.g. using the Cre-LoxP system)[51]. Furthermore, miRNA concentrations could be examined in preeclamptic animal models to detect if these miRNAs are also elevated in these models. If so, these animals could be treated to reduce these miRNA levels (by microRNA therapeutics) and investigate if this reduces the preeclamptic features like hypertension and proteinuria.

Conclusion

In conclusion, we demonstrated that early-onset preeclampsia is associated with changes in plasma miRNAs compared to healthy pregnancy. If this is also the case for late-onset preeclampsia, needs to be further investigated. Two of the most highly elevated miRNAs (miR-574-5p and miR-

1972) significantly influenced endothelial angiogenic function in our *in vitro* assays. We postulate that, besides the well-established pathways contributing to this multifactorial disease (e.g. signaling of sFlt-1, VEGF, inflammatory cytokines such as TNFα and the renin-angiotensin system) miRNAs may also contribute to the pathogenesis of preeclampsia, by affecting endothelial angiogenic cell function.

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600 Table 1. Patient information

	Non-pregnant women (n=10)	Healthy pregnancy (n=10)	Early-onset preeclampsia (n=10)
Age (years)	27.6 ± 4.5	28.0 ± 4.4	31.5 ± 5.7
Smoker (n)	0 (0%)	0 (0%)	1 (10%)
Nulliparous (n)	NA	8 (80%)	8 (80%)
Systolic blood pressure (mmHg)	NA	NR	168.0 ± 19.52
Diastolic blood pressure (mmHg)	NA	NR	104.3 ± 10.72
Urinary protein excretion (g/24h)	NA	NR	1.32 ± 1.71
Gestational age at sampling (weeks)	NA	29.8 ± 1.2	29.7 ± 2.8
Gestational age at delivery (weeks)	NA	40.3 ± 1.0	30.5 ± 2.6 ***
Newborn weight (g)	NA	3586 ± 291.6	1098 ± 368.0 ***
Perinatal mortality (n)	NA	0 (0%)	1 (10%)

601 Data are shown as mean ± SD or numbers (percentages). *** $p < 0.0001$ compared to healthy
602 pregnancy with unpaired t-statistics. NA = not applicable; NR = within normal ranges but not
603 routinely recorded.

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609 Table 2. Differentially expressed (precursor) miRNAs in early-onset preeclampsia vs. healthy
610 pregnancy.

	Fold change	False Discovery Rate
hsa-miR-1972_st	2.821007	1.58E-09
hsa-miR-574-5p_st	2.327063	6.99E-06
hsa-miR-1246_st	1.961194	0.048174
hsa-miR-4793-3p_st	1.860032	7.95E-05
hsa-miR-574-3p_st	1.761949	0.012838
hsa-miR-4745-5p_st	1.719226	0.019111
hsa-miR-4484_st	1.692787	0.036335
hsa-miR-1290_st	1.683642	0.036335
hsa-miR-1268_st	1.654545	0.012838
hsa-miR-3665_st	1.641798	0.0241
hsa-miR-4787-5p_st	1.600838	0.029235
hsa-miR-4436b-5p_st	1.494193	0.009999
hsa-miR-4440_st	1.431718	1.77E-05
hsa-miR-1910_st	1.417769	0.012838
hp_hsa-mir-1299_st	1.390918	3.13E-06
hsa-miR-4767_st	1.382612	0.024187
hsa-miR-1268b_st	1.366834	1.16E-05
hsa-miR-1207-5p_st	1.326744	0.02257
hp_hsa-mir-5095_st	1.303841	0.002187
hp_hsa-mir-4730_st	1.2653	0.0003
hsa-miR-4734_st	1.255385	0.040037
hp_hsa-mir-550b-2_s_st	1.250968	0.003634
hp_hsa-mir-4525_st	1.221849	0.003239
hsa-miR-3935_st	1.221763	0.030878
hp_hsa-mir-550b-1_s_st	1.206412	0.004849
hsa-miR-548a-3p_st	-1.32324	0.024187

611 MiRNA expression was measured by microarray
612

613 Table 3. Summary of studies investigating circulating miRNA concentrations before the onset of
614 preeclampsia or during preeclampsia as compared to healthy pregnancy

Study	Method for miRNA analysis	Number of PE patients included	Matrix	Type of preeclampsia	Main results in PE vs. healthy pregnancy
Wu et al.2012[23]	Mature miRNA microarray analysis and validation by RT qPCR	10	Plasma	Late-onset, severe preeclampsia	Increased miR-24, miR-26a, miR-103, miR-130b, miR-181a, miR-342-3p, and miR-574-5p
Munaut et al.2016[24]	MiRNAs were selected based on other articles and investigated by RT qPCR	23	Serum	Before the onset of preeclampsia (gestational age: 32.1 (25.3–36.6) weeks)	Increased miR-210-3p, miR-210-5p, miR-1233-3p, and miR-574-5p
Lu et al.2013[25]	SOLiD sequencing and validation by RT qPCR	16 mild PE and 22 severe PE	Plasma	Mild and severe preeclampsia	Increased miR-141 and miR-29a in mild PE and decreased miR-144 in both mild and severe PE
Ura et al.2014[26]	Microarray analysis and validation by RT qPCR	24	Serum	Before the onset of severe preeclampsia (gestational age: 12-14 weeks)	Increased miR-1233, miR-520, miR-210 and decreased miR-144
Jairajpuri et al. 2017[27]	Mature miRNA microarray consisting of miRNA probes targeting 84 PE associated genes	7 mild PE and 8 severe PE	Plasma	Mild and severe preeclampsia	Increased miR-215 miR-155, miR-650, miR-210 and miR-21 and decreased miR-18a, and miR-19b1

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Figure legends

Figure 1. Validation of the miRNA microarray. Real time quantitative PCR (RT qPCR) was performed to validate the miRNA expression values of the array data. Expression values of the three miRNAs which were mostly increased in concentrations were evaluated and the correlation between array and RT qPCR data was determined by Pearson correlation (A-C). Additionally, relative expression values of the miRNAs by RT qPCR were compared between PE (n=10), Pr (n=10) and NPr (n=10) groups (D-F). PE = early-onset preeclampsia; Pr = healthy pregnant; NPr = non-pregnant women. Data are presented as scatterplots including all data points. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by the Mann Whitney test.

Figure 2. Tube formation was assessed of endothelial cells transfected with miRNA mimics. Light microscopy pictures were taken after 12 h. Tube formation was quantified in the amount of loops formed (A), the total tube length (B) and total branching points (C). N=5. Data are presented as scatterplots including all data points. * $p < 0.05$ as compared with the control determined by one-sided Wilcoxon statistics.

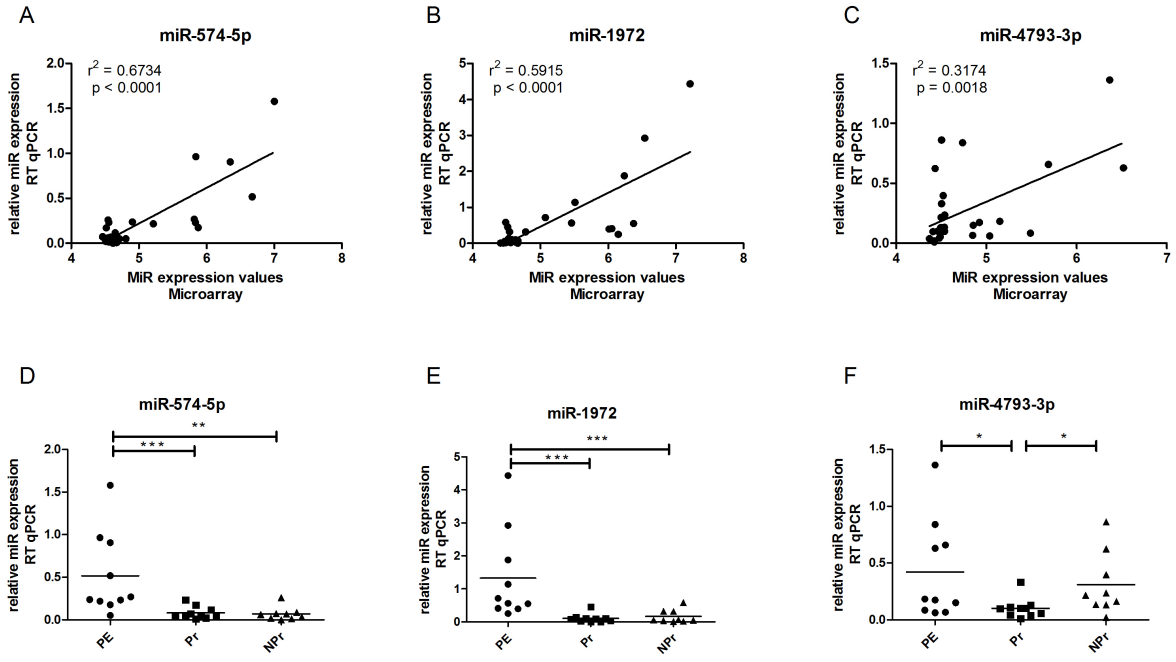
Figure 3. Wound healing was assessed of endothelial cells transfected with miRNA mimics. Light microscopy pictures were taken after 0, 4, 8, 12, and 24 h after the monolayer of cells had been scratched. Lines were drawn at the border of the scratch to clearly distinguish the wound area. Wound healing was quantified by the percentage of surface area closure (A) and the area under the curve (AUC) was calculated (B). N=5. Surface area closure is presented as median and interquartile range and the AUC is presented as a scatterplot including all data points. * $p < 0.05$ as compared with the control determined by one-sided Wilcoxon statistics.

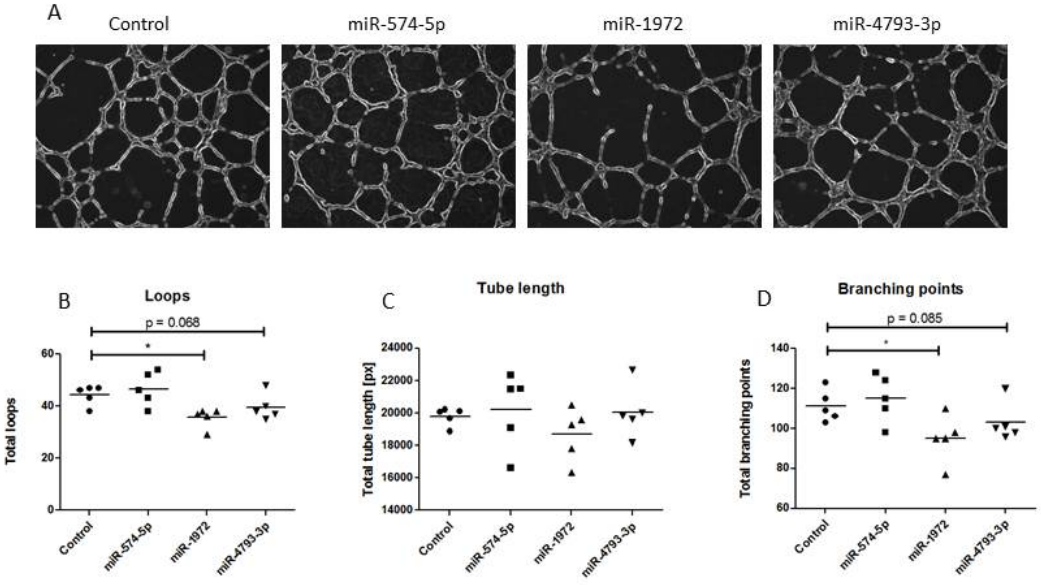
Figure 4. Proliferation was assessed of endothelial cells transfected with miRNA mimics by the WST-1 assay.

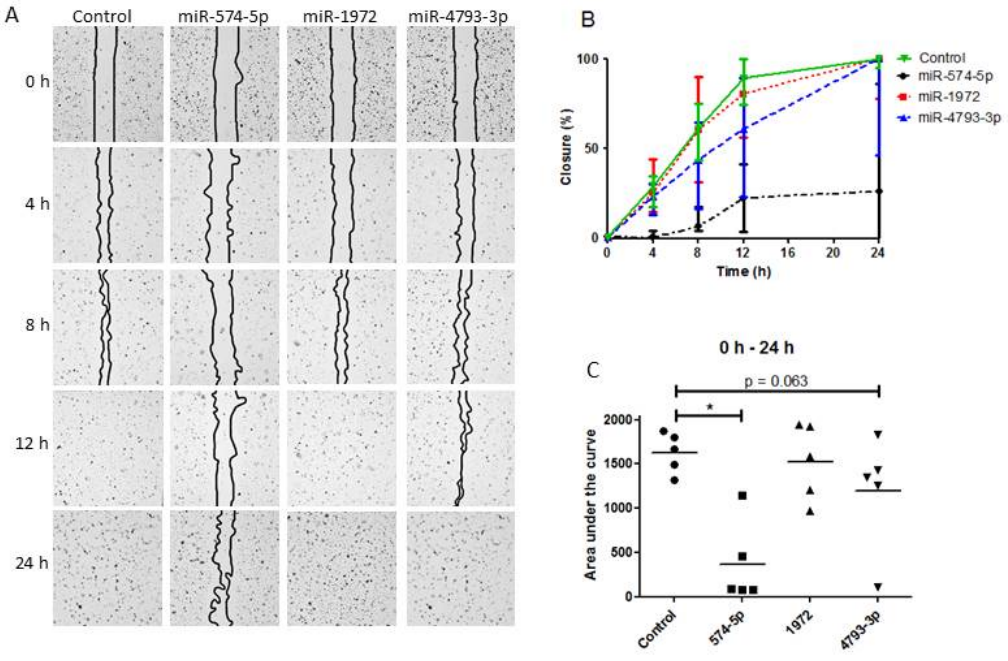
643 N=5. Data are presented as scatterplots including all data points. Significance was determined by
644 one-sided Wilcoxon statistics.

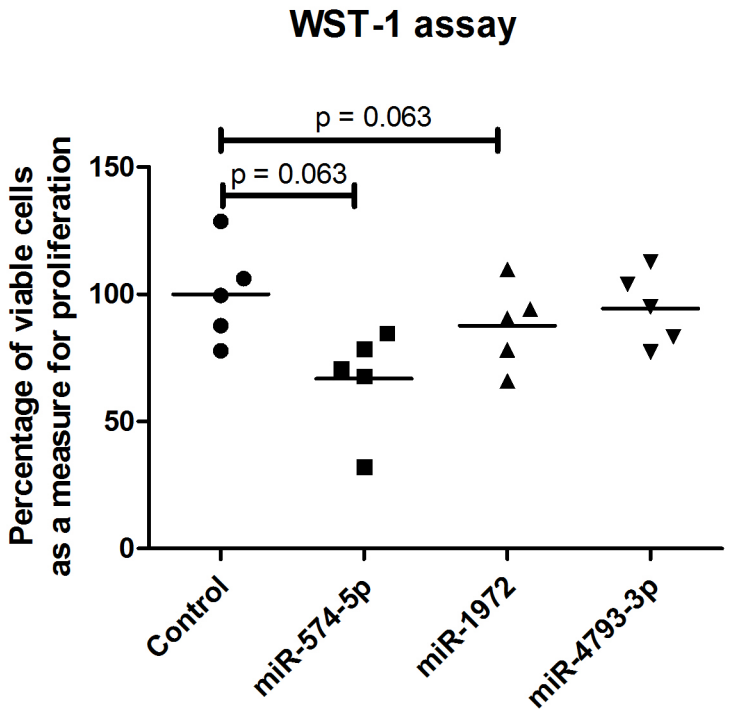
645

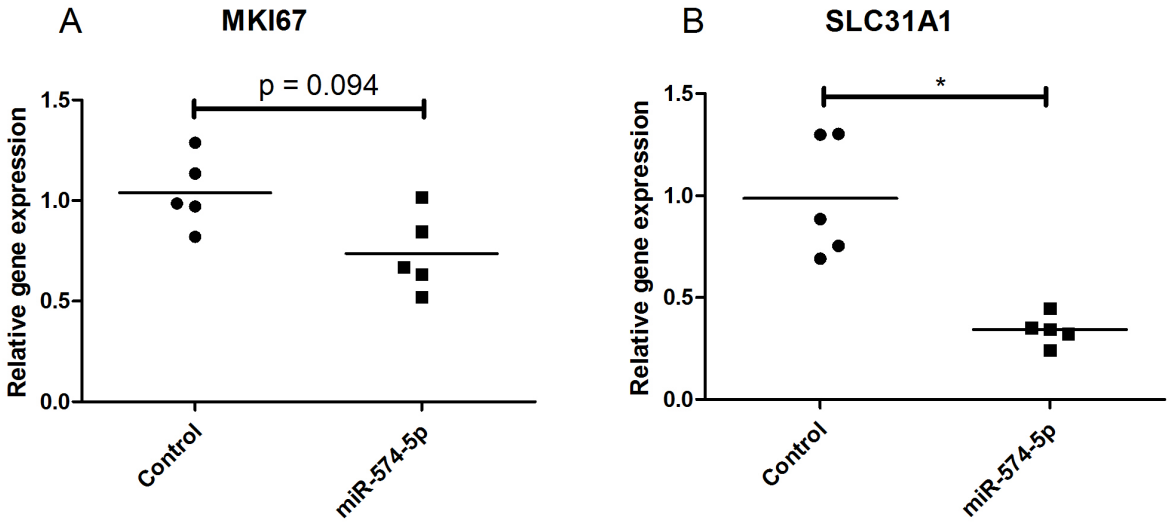
646 Figure 5. Targets of miR-574-5p were examined by real time quantitative PCR. Relative gene
647 expression of *MKI67* (A) and *SLC31A1* (B) in endothelial cells transfected with the miR-574-5p mimic
648 were evaluated. N=5. Data are presented as scatterplots including all data points. * $p < 0.05$ as
649 compared with the control by one-sided Wilcoxon statistics.


A
miR-574-5p
r2 = 0.6734
p < 0.0001
relative miR expression RT qPCR
MiR expression values Microarray
B
miR-1972
r2 = 0.5915
p < 0.0001
relative miR expression RT qPCR
MiR expression values Microarray
C
miR-4793-3p
r2 = 0.3174
p = 0.0018
relative miR expression RT qPCR
MiR expression values Microarray
D
miR-574-5p
relative miR expression RT qPCR
PE
Pr
NPr
E
miR-1972
relative miR expression RT qPCR
PE
Pr
NPr
F
miR-4793-3p
relative miR expression RT qPCR
PE
Pr
NPr


A
Control
miR-574-5p
miR-1972
miR-4793-3p
B
Loops
p = 0.068
*
Total loops
60
40
20
0
Control
miR-574-5p
miR-1972
miR-4793-3p
C
Tube length
Total tube length [px]
24000
22000
20000
18000
16000
14000
Control
miR-574-5p
miR-1972
miR-4793-3p
D
Branching points
p = 0.085
*
Total branching points
140
120
100
80
60
Control
miR-574-5p
miR-1972
miR-4793-3p


A
Control
miR-574-5p
miR-1972
miR-4793-3p
0 h
4 h
8 h
12 h
24 h
B
Control
miR-574-5p
miR-1972
miR-4793-3p
Closure (%)
Time (h)
C
0 h - 24 h
p = 0.063
*
Area under the curve
Control
574-5p
1972
4793-3p





Supplementary File

Early-onset preeclampsia, plasma microRNAs and endothelial cell function

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Supplemental Materials and Methods

Study design and rational

In the first part of this study, plasma miRNA concentrations of early-onset preeclamptic patients are compared with plasma microRNA concentrations of healthy pregnant and non-pregnant women. This was done by miRNA microarray technologies. Three miRNAs with the highest fold change (fold change > 1.8) and with a false discovery rate < 0.01 in preeclamptic as compared to healthy pregnant plasma were validated by real-time quantitative PCR. These three miRNAs were also selected for further investigation in the second part of the study.

In the second part of the study we examined the effects of increasing the concentrations of the selected miRNAs in endothelial cells. To increase miRNA concentrations in endothelial cells, endothelial cells were transfected with miRNA mimics (chemically modified RNAs that mimic endogenous miRNAs). Subsequently, assays were performed to assess endothelial cell function *in vitro*. These assays include a tube formation assay, a wound healing assay and a proliferation assay. The tube formation assay is a well-established model for measuring formation of endothelial cell tubes, which is part of the angiogenesis process *in vitro*[1]. The other two assays also assess processes that are important for angiogenesis[2]. The wound healing assay assesses migration/proliferation of

cells after insertion of a linear scratch in the cell monolayer[3]. The proliferation assay measures proliferation of the cells, by measuring metabolic activity of the transfected cells over time.

Since miRNAs functions by decreasing mRNA expression, in the last part of this study it was investigated if the miRNAs were able to indeed modify gene expression pattern in the transfected endothelial cells. To do so, mRNA expression of the endothelial cells was characterized by gene expression microarray and validated by real-time quantitative PCR.

Patient recruitment and plasma collection

The sample size of 10 subjects in each group was decided using power calculations described in the article of Liu et al[4]. Preeclampsia was defined according to the definition from the Practice Bulletin #203 "Chronic Hypertension in Pregnancy": a systolic blood pressure of ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg on two or more occasions at least 4 h apart after 20 weeks of gestation in women with a previously normal blood pressure, and proteinuria ≥ 300 mg/24 h[5]. Samples included in this study were from early-onset preeclampsia, these women all delivered before week 34 of gestation and did no show comorbidities, such as autoimmune diseases (i.e. diabetes, antiphospholipid syndrome, SLE) or chronic hypertension. Non-pregnant women included were personnel at the UMCG, and healthy pregnant women were recruited from the midwifery antenatal clinics at the UMCG. PE patients were recruited from patients admitted in the UMCG. Blood was drawn from the antecubital vein into tubes containing EDTA (BD Biosciences). healthy pregnant women and PE were matched for gestational age at sampling. For non-pregnant women, samples were obtained within 10 days from the start of last menstruation. Within 1 h, samples were centrifuged at 4°C, 130 g for 10 min followed by 700 g for 10 min. Plasma was stored at -80°C until further use. The medical ethical committee of the UMCG approved this study, and informed consent was signed by all participants.

RNA isolation

Total RNA was isolated from the plasma samples with TRIzol reagent (Invitrogen), followed by RNA purification with the miRNeasy Serum/plasma kit (Qiagen) according to manufacturer's instructions. RNA quality was assessed by the Qubit Fluorometer using the Qubit microRNA Assay Kit (Life Technologies).

MicroRNA array

Total RNA (1 µg) was labelled with the use of the Affymetrix FlashTag Biotin HSR RNA Labeling kit (P/N 901911, Affymetrix) and hybridized to miRNA 3.1 arrays targeting 3,391 human (precursor) microRNAs ((pre-)miRNAs) (P/N 90215, Affymetrix). The miRNAs targeted by this array were all (precursor) miRNAs known at that moment (100% miRBase v17 coverage). Sample labelling, hybridization to chips and image scanning was performed according to the manufacturer's instructions (for detailed protocols: Affymetrix FlashTag Biotin HSR RNA Labeling Kit User Manual (P/N 703095, Revision 2)).

Before statistical analysis, the quality of the datasets obtained from the scanned Affymetrix arrays was determined. Quality control of the data was performed using Bioconductor packages[6] integrated in an on-line pipeline[7]. Various advanced quality metrics, diagnostic plots, pseudo-images and classification methods were applied[8]. Background correction, normalization and summation of the miRNA arrays was performed as described before[9] with minor modifications. In brief: background was corrected by a robust normal-exponential convolution model that takes into account the intensities of the negative control probes present on the array. This was followed by weighted cyclic loss normalization for all probes. To this end, all control probes (except the negative controls) were assigned weight 100, and all other probes, including those detecting (pre-)miRNAs, 5.8 rRNA and small nucleolar RNAs (including small Cajal body-specific RNAs and C/D box and H/ACA box small RNAs) were attributed a weight of 0.001. Finally, probes were summarized into probe set expression estimates[9].

MicroRNA array data analysis

The differentially expressed probe sets were identified using linear models, applying moderated t-statistics that implemented intensity-dependent empirical Bayes regularization of standard errors[10,11]. The moderated t-test statistic has the same interpretation as an ordinary t-test statistic, except that the standard errors have been moderated across genes, i.e. shrunk to an intensity-dependent common value, using a Bayesian model. P-values were corrected for multiple testing using a false discovery rate method[12]. Probe sets with a fold change of > 1.2 or < -1.2 and a false discovery rate < 0.05 were considered significantly different. For further analysis, the miRNAs with the highest fold change (fold change > 1.8 with a false discovery rate < 0.01) in PE vs. healthy pregnant women were chosen (miR-574-5p, miR-1972 and miR-4793-3p).

MicroRNA array validation by real-time quantitative PCR

Validation of the array was done by real-time quantitative PCR (RT qPCR) using miRNAs which were found to change with the highest fold change and with tha false discovery rate < 0.01 in preeclampsia (miR-574-5p, miR-1972 and miR-4793-3p). From total RNA, which was also used on the miRNA array, cDNA was prepared with the TaqMan Advanced miRNA cDNA synthesis Kit (Applied Biosystems) following manufacturer's instructions. To measure miRNA expression, TaqMan advanced miRNA assays (Applied Biosystems) were used (Supplementary Table 1). RT qPCR was performed using 2.5 µL of 10x diluted cDNA, 2 µL RNase-free water, 0.5 µL TaqMan Advanced miRNA assay, and 5 µL TaqMan Fast Advanced Master Mix (Applied Biosystems). Samples were run in triplicates on a StepOnePlus™ Real-Time PCR System machine (Applied Biosystems) with the following protocol: 20 s 95°C, followed by 40 cycles of 3 s 95°C and 30 s 60°C. Relative expression levels were calculated by the $2^{-\Delta CT}$ method and normalized against expression levels of the relatively stable endogenous control hsa-miR-191-5p.

Human umbilical vein endothelial cell culturing

Isolation of human umbilical vein endothelial cells was performed in the endothelial cell facility of the UMCG using umbilical veins from term pregnancies without complications (such as autoimmune diseases, preeclampsia and intra uterine growth restriction) and cells were pooled from at least 2 donors and cultured as described before[13]. The cells were cultured on 1% gelatin coated flasks at 37°C, 5% CO_2 in endothelial cell medium (ECM). ECM consisted of RPMI 1640 (Lonza) supplemented with 20% heat inactivated fetal calf serum (Sigma), 2 mM L-glutamine (Lonza), 1% gentamicin (Lonza), 5 U/mL heparin (Leo Pharma), and 50 µg/mL endothelial cell growth factors supplement extracted from bovine brain (which was prepared using the method of Maciag et al.[14]). endothelial cells were used at passage 3.

Transfection of endothelial cells with miRNA mimics

50% confluent endothelial cells (passage 3) were transfected with *mir*Vana miRNA mimics (miR-574-5p, miR-1972 or miR-4793-3p) or the *mir*Vana miRNA mimic negative control #1 (Ambion) in 12-wells and 96-wells plates. Transfected endothelial cells in 12-wells plates were used for the tube formation assays, the wound healing assays and RNA isolation, and transfected endothelial cells in 96-wells plates were used for the proliferation assays.

For 12-wells plates: 9 µL Lipofectamine RNAiMAX transfection reagent (Invitrogen) was diluted in 150 µL Opti-MEM Medium (Life Technologies) and 30 pmol miRNA mimic was diluted in 150 µL Opti-MEM medium. The two solutions were mixed and incubated for 5 min. Then, 100 µL miRNA-lipid mixture was added (dropwise) to each well. Cells were incubated for 48 hours at 37°C, 5% CO_2.

For 96-wells plates: 1.5 µL Lipofectamine was diluted in 25 µL Opti-MEM medium and 5 pmol miRNA mimic was diluted in 25 µL Opti-MEM medium. The two solutions were mixed and incubated for 5 min. Then, 10 µL miRNA-lipid mixture was added to each well. Cells were incubated for 48 hours at 37°C, 5% CO_2.

Tube formation assay

The tube formation assay is a well-established model for measuring tube formation, i.e. the ability of the endothelial cells to form capillary-like structures *in vitro*. This is part of the angiogenic process[1]. Matrigel basement membrane matrix (Corning) was defrosted at 4°C overnight. 10 µL of matrigel was pipetted with precooled pipet tips into the inner wells of the µ-Slide Angiogenesis (Ibidi). Slides were incubated for 45 min at 37°C. The transfected endothelial cells were collected after 48 h of incubation following trypsin (Gibco) treatment. 10,000 endothelial cells dissolved in 50 µL ECM were seeded into each well of the µ-Slide Angiogenesis on top of the matrigel. After 12h of incubation at 37°C, 5% CO_2, pictures were taken with the Leica MC120 HD (Leica Microsystems). Tube formation was quantified as total amount of loops (i.e. numbers of capillaries formed), total tube length (length of the capillaries) and total branching points (number of interconnections between the tubules, which gives information on how endothelial cells organize themselves) by using Wimasis, 2017 (n=5). (WimTube: Tube Formation Assay Image Analysis Solution. Release 4.0. Available from: https://www.wimasis.com/en/products/13/WimTube).

Wound healing assay

Endothelial cell migration and/or proliferation potential was assessed by the wound healing assay of the transfected endothelial cells in a 12-wells plate. A linear scratch was made using a sterile 200 µL pipet tip. The wells were washed twice with PBS to remove debris followed by ECM replacement. The microscope was used to confirm scratches were comparable in all groups and wells did not contain cell debris. Pictures were taken with the Leica MC120 HD (Leica Microsystems) of the same area of the scratch after 0, 4, 8, 12, and 24 h of incubation at 37°C, 5% CO_2. To measure how long it takes to close the wound, the surface area of the scratch was measured using ImageJ (n=5).

WST-1 assay for cell proliferation

Since the wound healing assay evaluates both migration and proliferation, but does not allow discrimination between these processes, we also performed a proliferation assay, which specificallymeasures proliferation of the cells. To do so, the metabolic activity of transfected endothelial cells was measured by colorimetric WST-1 assays (4-[3-(4-Iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate) (cat. no. 05015944001; Roche Applied Science). 50% confluent endothelial cells in a 96-wells plate were transfected in triplicates as described above. 48 hours after transfection, 10 µl WST-1 solution was added to culture medium in all wells. As a blank, culture medium (without cells) was incubated with WST-1 solution. The samples were incubated for 2h at 37°C. Subsequently, the plate was thoroughly shaken for 1 min and absorbance was measured at 450 and 750 (background) nm. The WST-1 assay measures the number of viable cells. An increase in the number of viable cells indicates proliferation, a decrease of the number of viable cells indicates cell death. This was calculated with the use of the following formula: (Absorbance 450 nm – Absorbance 750)/(Absorbance control 450 nm – Absorbance control 750 nm)*100. N=5

RNA isolation and gene expression microarray of transfected endothelial cells

To identify miRNAs targets in endothelial cells, total RNA was isolated from transfected endothelial cells and gene expression was evaluated by microarray. Total RNA was isolated with the use of AllPrep DNA/RNA Mini Kit (Qiagen) according to manufacturer's instructions. RNA quality was assessed using RNA 6000 nanochips on the Agilent 2100 bioanalyzer (Agilent Technologies, Amstelveen, the Netherlands).

Gene expression microarray was performed with pooled samples from 6 independent experiments. Four pooled samples were tested: endothelial cells transfected with the control miRNA and endothelial cells transfected with the miR-574-5p, miR-1972 or miR-4793-3p mimics. Total RNA (100 ng) was labelled using an Affymetrix WT plus reagent kit and hybridized to whole genome Genechip Human Gene 2.1 ST arrays coding 25.088 genes and transcripts, (Life Technologies, the Netherlands). Sample labelling, hybridization to chips and image scanning was performed according

manufacturer's instructions. Microarray analysis was performed using MADMAX pipeline for statistical analysis of microarray data[6]. Quality control was performed and all arrays met our criteria. For further analysis a custom annotation was used based on reorganized oligonucleotide probes, which combines all individual probes for a gene[15]. Expression values were calculated using robust multichip average (RMA) method, which includes quantile normalisation[16]. Since the array was performed with one pooled sample per group, no further statistics were performed.

RT qPCR of potential miRNA targets

To confirm the potential targets of the miRNAs identified by microarray, RT qPCR was used. Total RNA (up to 1 µg in 10 µL) was reverse transcribed using M-MLV Reverse Transcriptase (Invitrogen) and random nonamers (Sigma), following manufacturer's instructions. cDNA was diluted 1:10 and stored at -20°C until further use. RT qPCR was performed using 2 µL cDNA, 5 µL PowerUp™ SYBR™ Green Master Mix (Life Technologies), 0.125 µL µL (10 µM) forward and reverse primer mix, and 2.875 µL RNAse free water. Samples were run in triplicates on a StepOnePlus™ Real-Time PCR System machine (Applied Biosystems) with the following protocol: 2 min 50°C, 2 min 95°C, followed by 40 cycles of 3 sec 95°C, 30 sec 60°C. Primers (Invitrogen) were designed using Primer3 and BLAST (Supplementary Table 2). Relative expression levels were calculated by the $2^{-\Delta CT}$ method and normalized against expression levels of *36B4*.

Statistics

The data were analyzed with Graphpad Prism 5.0. Normality of the data was examined by the D'Agostino-Pearson normality test. Patient information analysis of continuous variables are presented as mean ± SD and significance was determined by unpaired t-statistics, and analysis of categorical variables were presented as numbers (percentages) and significance was determined by chi-square and Fisher's exact test. Correlations between microRNA array and RT qPCR expression values were determined by Pearson correlation. RT qPCR data of microRNA array data validation are

presented as scatterplots including all data points and significance was determined by the one-tailed Mann Whitney test. Tube formation, the AUC of the wound healing, WST-1 and RT qPCR data of transfected endothelial cells are presented as scatterplots including all data points and significance was determined by one-tailed Wilcoxon statistics. $P < 0.05$ was considered significant and $p < 0.1$ was considered a trend.

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Supplementary Tables 1 and 2

Early-onset preeclampsia, plasma microRNAs and endothelial cell function

Simone V. LIP, MSc, Mark V. BOEKSCHOTEN, PhD, Guido J. HOOIVELD, PhD, Mariëlle G. VAN PAMPUS, MD, PhD, Sicco A. SCHERJON, MD, PhD, Torsten PLÖSCH, PhD, Marijke M. FAAS, PhD

Supplementary Table 1. TaqMan Advanced miRNA assays (Applied Biosystems)

TaqMan Advanced miRNA assay	Catalog number
hsa-miR-191-5p	A25576/477952-mir
hsa-miR-574-5p	A25576/479357-mir
hsa-miR-1972	A25576/478746-mir
hsa-miR-4793-3p	A25576/480053-mir

Supplementary Table 2. RT qPCR Primers

	Forward primer	Reverse primer
36B4	GCTTCATTGTGGGAGCAGACA	CATGGTGTTCTTGCCCATCAG
MKI67	GACTTTGGGTGCGACTTGAC	ACAACTCTTCCACTGGGACG
SLC31A1	ACCATCACCCAACCACTTCA	AAAAGCTCCAGCCATTTCTCC

Supplementary tables 3 through 5

Early-onset preeclampsia, plasma microRNAs and endothelial cell function

Simone V. LIP, MSc, Mark V. BOEKSCHOTEN, PhD, Guido J. HOOIVELD, PhD, Mariëlle G. VAN PAMPUS, MD, PhD, Sicco A. SCHERJON, MD, PhD, Torsten PLÖSCH, PhD, Marijke M. FAAS, PhD

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
SLC31A1	899.49823	69.45847676	-12.95015766
DCAKD	461.58199	55.04372557	-8.385733146
GLYR1	1078.3701	128.8975559	-8.366101782
BMP4	1630.8149	205.2963157	-7.943712687
SIGMAR1	1504.1313	198.3874051	-7.581788087
PORCN	203.22358	27.05365032	-7.511872677
ESCO2	193.07599	28.71375495	-6.72416365
KIAA0895L	115.04248	17.413865	-6.606372771
MIR4653	27.636899	4.192818114	-6.591485368
MCM8	417.68586	65.52715183	-6.374241035
CALCOCO1	145.69318	25.47558657	-5.718933239
ZNF774	44.77574	8.104864742	-5.524551172
SCARA3	316.09452	61.64403208	-5.127739151
EHD3	68.983271	13.55810492	-5.087972969
XRCC1	560.68105	110.4487965	-5.076388929
SNX2	882.44662	176.2003376	-5.008200505
LHFP	295.09312	61.71754131	-4.781349235
MIR3127	15.376813	3.234001074	-4.754733494
OR4N2	15.507999	3.271322692	-4.740589814
LOC101927093	12.016116	2.674727534	-4.492463551
CTSD	2175.8256	493.9523125	-4.404930517
TRIOBP	55.070719	12.50717907	-4.403128704
CLEC18B	34.608425	7.935935743	-4.36097598

Supplementary table 4

Gene	Control	miR-1972	Fold change
RSAD2	87.232357	10.4733628	-8.328973071
CXCL10	76.013852	9.56796814	-7.944618026
PPP3CB-AS1	27.810221	4.47922747	-6.208709294
MIR548AL	18.951217	3.05522005	-6.202897499
MIR1254-1	17.193305	2.90227128	-5.924085987
IFI44L	181.84091	33.0556447	-5.501054569
LOC100506113	17.535078	3.31088732	-5.296186942
OR4N2	15.507999	2.96043059	-5.238426825
MX2	37.871554	8.17292792	-4.633780534
MX1	334.73261	79.6641826	-4.20179563
IFIT1	29.641818	7.08253608	-4.185198331
IGHV3-16	24.882514	6.10911403	-4.073015118
SLC22A1	106.34636	26.8411744	-3.962060516
HS3ST2	28.864616	7.48206536	-3.857840634
NA	14.532512	3.82406615	-3.800277323
GOLGA6A	25.396446	6.80025542	-3.734631127
LINC01260	9.4270466	2.53968394	-3.711897537
PPIAL4C	9.0359666	2.44901409	-3.689634382
RAET1G	27.577317	7.79961655	-3.535727312
LOC400743	26.780546	7.58494542	-3.530750054
NA	10.814676	3.18423614	-3.396317061
OAS2	95.583231	28.6991887	-3.330520304
PRAMEF7	13.846143	4.16422751	-3.325020854

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
RSAD2	87.232357	8.556116505	-10.1953213
CXCL10	76.013852	11.35855176	-6.692213393
IFI44L	181.84091	30.31751532	-5.997882856
MX2	37.871554	6.366703933	-5.948376854
OASL	48.895642	9.63893179	-5.072724127
LOC100996713	11.926805	2.372280512	-5.027569257
MX1	334.73261	69.03828458	-4.848507118
IFIT1	29.641818	6.669024176	-4.444700961
RRN3P2	16.248763	4.148192414	-3.917070598
OR4N2	15.507999	4.067342069	-3.812809144
GOLGA8R	24.619413	6.57016392	-3.747153549
LOC101928160	14.153222	3.80042909	-3.724111605
PRRX2	31.033179	8.764420814	-3.540813443
EPSTI1	27.372585	7.746830566	-3.533391515
CGB1	16.057483	4.568679989	-3.514687717
IFITM1	611.07204	184.8602771	-3.305588686
FAM47B	15.210835	4.651187936	-3.270311809
SLC22A1	106.34636	32.78994514	-3.243261213
FDPSP2	11.420594	3.571584422	-3.197626855
LOC101927762	22.714008	7.152978454	-3.175461509
NA	21.947702	7.024515415	-3.124443521
KRTAP20-2	29.285164	9.407116652	-3.113086108
NA	15.617896	5.050272526	-3.092485837

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
NCK2	506.24467	117.1353184	-4.321878944
TMEM150C	57.003504	13.34414954	-4.271797452
SPTLC3	36.287062	8.585133369	-4.226732474
SNAI2	65.446929	15.50225602	-4.221768021
FAM117B	322.83775	78.81760835	-4.096010456
SLC43A3	1533.7455	382.6967687	-4.007730544
EDA2R	132.49263	33.50626944	-3.954263808
PPP1R16B	505.55973	131.8694098	-3.833790816
RAET1G	27.577317	7.376570217	-3.738501289
LOC101929380	12.992967	3.508208088	-3.703590714
ZSWIM1	76.957672	21.05383646	-3.655280237
HPS3	765.60496	211.2813123	-3.623628397
NA	15.617896	4.349743407	-3.590532774
SERPINB9P1	138.37636	39.64631799	-3.490270071
PTPLAD1	1488.6247	428.9483349	-3.470405489
LOC101928160	14.153222	4.093040962	-3.457874527
NA	21.947702	6.428630225	-3.414055702
BTN3A3	10.992588	3.231265398	-3.401945233
EFNB1	210.44441	61.86728806	-3.401545718
MIR486-1	26.263357	7.732655566	-3.396421364
ZNF449	77.667366	22.95056775	-3.384115253
FAM47B	15.210835	4.506569428	-3.375258071
FAM86C1	71.744202	21.28216871	-3.371094515
MIR1238	22.187246	6.668705734	-3.327069313
TRBV7-6	18.564897	5.594803746	-3.318239219
PTTG1	50.47561	15.23519831	-3.313091759
KLF7	794.41648	244.577569	-3.248116663
SKA2	80.570813	25.42606769	-3.168827137

Supplementary table 4

Gene	Control	miR-1972	Fold change
LOC101927762	22.714008	6.83984866	-3.320834842
SNRPE	16.478113	4.96397653	-3.319538801
OAS1	156.23063	48.7231262	-3.206498467
EPSTI1	27.372585	8.56251927	-3.1967911
IFITM1	611.07204	191.233018	-3.195431656
LOC101927093	12.016116	3.85417925	-3.117684772
LOC101928219	12.797946	4.10758559	-3.115685838
LOC286297	18.557671	5.9886268	-3.098819131
IL12A	13.322684	4.36347451	-3.053228444
LOC101927751	38.62771	12.689797	-3.043997494
DEFB4B	9.423337	3.12702978	-3.013510473
NA	21.947702	7.31334771	-3.001047201
LOC100288798	23.588847	7.86617374	-2.998770204
FAM47B	15.210835	5.07619927	-2.996500733
LOC101929236	27.750622	9.36962962	-2.961762989
FCN2	7.0788299	2.43301978	-2.9094831
IFI6	738.78338	257.257814	-2.871762649
MIR4689	15.271899	5.35900587	-2.849763434
OASL	48.895642	17.2516165	-2.834264366
MFI2	32.289194	11.4614748	-2.817193682
LOC101927614	28.168854	10.3139568	-2.731139477
IFIT3	69.103881	25.3052095	-2.73081639
BMP8B	11.195419	4.12330367	-2.715157647
TRBV7-6	18.564897	6.89653195	-2.691917813
FAM106B	45.828554	17.1468881	-2.672703834
AKR7A2	41.303951	15.5124341	-2.662635075
LOC254896	51.921316	19.5662682	-2.653613621
RSPH10B	7.4606891	2.81673287	-2.648703105

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
RSPH10B	7.4606891	2.422810944	-3.079352568
TRAF1	220.12821	71.59448765	-3.074653024
LOC100506113	17.535078	5.734615504	-3.057760054
VTRNA2-1	31.880586	10.43953574	-3.05383176
LOC101928716	13.791835	4.52391271	-3.048651785
IFI6	738.78338	244.1768013	-3.025608405
TRBV7-6	18.564897	6.162802398	-3.012411565
IFIT3	69.103881	23.01589632	-3.002441437
OAS2	95.583231	32.34486893	-2.955128085
MRGPRD	23.46354	7.96204312	-2.946924448
PSG4	11.156337	3.786009139	-2.946727479
MIR548AL	18.951217	6.47672684	-2.926048493
SPX	53.909972	18.77317317	-2.871649425
NA	14.532512	5.06139225	-2.871247899
TTTY20	11.532613	4.096326454	-2.815354852
CCL20	550.19478	199.4021336	-2.759222146
LOC100506217	14.174572	5.238748097	-2.705717431
LINC00937	14.096305	5.25277164	-2.683593721
SPATA31C1	15.987191	5.990012838	-2.668974427
LOC645513	21.94902	8.228457757	-2.667452441
REG1A	7.1451142	2.683534409	-2.662575947
LOC101928859	10.40721	3.914013283	-2.658961407
LOC389705	11.593037	4.373967738	-2.650462368
HS3ST2	28.864616	10.90031459	-2.648053459
PYGM	13.541365	5.13659898	-2.636251206
LOC101927300	13.206683	5.03964344	-2.62055896
LOC101927144	11.880177	4.571753657	-2.598604028
RAB3IL1	79.178687	30.48705529	-2.597124788

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
LOC400743	26.780546	8.532649199	-3.138596915
MIR548AL	18.951217	6.095993045	-3.108798956
LINC00937	14.096305	4.611086836	-3.057046092
UBLCP1	608.9842	200.1592195	-3.042498873
KRTAP20-2	29.285164	9.798382446	-2.988775374
MYZAP	33.903223	11.38710451	-2.977334834
HAGLR	47.807018	16.10406336	-2.968630757
ANG	77.250331	26.07516135	-2.962602219
OR10S1	10.080532	3.409606714	-2.956508735
LCE3B	29.609679	10.05948094	-2.943459912
RPL23AP7	10.111639	3.441351147	-2.938275955
HOXA2	51.407804	17.65206883	-2.912282122
NA	77.459186	26.92001183	-2.877383062
GSTM2	12.356682	4.305218494	-2.870163643
LINC01260	9.4270466	3.314637454	-2.844065664
AQP1	28.656526	10.14265431	-2.82534782
LOC101929432	13.784772	4.891967184	-2.817838175
MIR520F	9.5227824	3.402136435	-2.799059539
LOC100288798	23.588847	8.537143173	-2.763084438
RPS10	28.597101	10.53143614	-2.715403707
FAXDC2	108.79567	40.06746878	-2.715311664
GOLGA6A	25.396446	9.390491847	-2.704485129
MARCH3	707.35591	262.330525	-2.69643005
LINC01197	206.29273	76.72874826	-2.688597596
SLC10A5	14.215453	5.295706027	-2.684335682
LOC101928859	10.40721	3.87708654	-2.684286296
GPBP1L1	381.74035	142.5044375	-2.678796247
CAMK2N1	158.13998	59.27865739	-2.667738963

Supplementary table 4

Gene	Control	miR-1972	Fold change
ALPP	9.8710223	3.74173012	-2.638090396
MIR519A1	7.9139383	3.00015261	-2.637845253
CSRP2BP	17.688123	6.71994044	-2.632184505
LINC01180	10.114726	3.8611913	-2.619586873
POM121L10P	22.869521	8.75178993	-2.613125047
HIST1H2BH	22.896161	8.84449647	-2.588746658
TCEB3CL2	15.498478	6.0149609	-2.576654838
CLEC18B	34.608425	13.4878136	-2.565903278
C8orf88	26.138486	10.2967997	-2.538505856
MAGEA4	10.062814	3.98288013	-2.526516947
IFNA4	6.7784289	2.68473112	-2.524807346
ZNF324	23.956015	9.51219591	-2.518452681
LOC100289061	34.271702	13.6148896	-2.517222153
ZP3	15.782153	6.35708632	-2.48260801
LOC101928716	13.791835	5.56878391	-2.476633098
ZNF90	38.766252	15.6637141	-2.474908054
ZNF506	10.630432	4.32971433	-2.455227185
SNORD115-24	8.0006711	3.26052291	-2.453800001
IGKV3D-11	9.6125009	3.938251	-2.440804543
C8orf31	12.22449	5.04858295	-2.421370616
ATP1A3	13.273697	5.50810277	-2.409849212
FOS	36.085853	14.9797056	-2.408982816
PYGM	13.541365	5.63276117	-2.404036821
LOC101929463	9.9281657	4.1376526	-2.399468177
TRAJ59	12.598117	5.25077756	-2.399286058
LOC100507334	14.335607	5.9986639	-2.389800065
MIR4292	16.460554	6.93373041	-2.37398246
MIR4674HG	17.479948	7.43246062	-2.351838592

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
LINC01491	8.4059163	3.242125567	-2.592717682
UGT2A1	8.3758392	3.233123057	-2.590634219
LINC01260	9.4270466	3.641924529	-2.588479386
OAS1	156.23063	60.78200405	-2.570343505
LINC01180	10.114726	3.946072876	-2.563238532
CTC-338M12.4	37.366622	14.65615633	-2.549551254
MIR3163	24.962528	9.820578689	-2.541859216
CCL5	48.886391	19.3307745	-2.528941138
CSF2	24.659026	9.754471078	-2.52797164
LOC101927614	28.168854	11.15204931	-2.525890415
LOC101929380	12.992967	5.172236065	-2.512059916
NA	15.493125	6.196815862	-2.500175222
ALG10B	11.202913	4.484961776	-2.497883686
BOLA3-AS1	42.085855	16.85882224	-2.496369825
LINC00702	36.317201	14.55117281	-2.495826384
MIR486-1	26.263357	10.53246907	-2.493561234
MYHAS	13.270634	5.362987117	-2.47448561
SRP54-AS1	19.60325	7.946566041	-2.466883221
LOC100996671	7.4291028	3.021553118	-2.458703351
KRT33B	9.7461771	3.972692468	-2.453292607
LOC101926893	8.6738539	3.538372512	-2.451368201
KCNK15	8.1159598	3.320847684	-2.443942211
EBI3	22.105568	9.06051256	-2.439770189
CCDC144CP	12.791317	5.246921821	-2.4378707
LOC101927307	11.172323	4.583127807	-2.437707131
C2orf70	18.304238	7.510438829	-2.43717295
CNR1	20.289823	8.366271914	-2.425192906
CTU1	40.877987	16.86416519	-2.423955591

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
FGFRL1	87.340343	32.76716725	-2.665483467
OSBPL9	812.54631	305.0994924	-2.663217515
C10orf10	638.34631	240.4534957	-2.654759938
LOC101928219	12.797946	4.834366532	-2.64728505
TP53I11	60.772083	23.00256046	-2.641970359
GCNT3	10.917253	4.149315101	-2.631097492
MIR519A1	7.9139383	3.025533277	-2.615716836
PPIAL4C	9.0359666	3.454746489	-2.615522331
SEPT6	215.41051	83.22804726	-2.58819608
MIR196B	54.487592	21.05419869	-2.587967998
SENP1	702.83381	271.5797778	-2.587946039
SELENBP1	68.453233	26.51502921	-2.58167668
CCDC88C	107.90656	41.82270461	-2.580095289
LOC100653133	21.809327	8.522237032	-2.559108236
E2F8	147.53756	58.03560045	-2.542190555
GJA4	33.09791	13.11817547	-2.523057426
ANO8	33.075704	13.11274623	-2.522408592
OR10G8	12.742403	5.056019041	-2.520244314
DKFZp779M0652	20.45614	8.170782165	-2.503571846
CD93	1581.7864	632.0408767	-2.502664724
FLJ20021	48.804657	19.62879293	-2.486380955
SNORD114-14	39.890121	16.06297751	-2.483357801
PRAMEF7	13.846143	5.593566117	-2.475369561
MAL2	200.09982	80.8818977	-2.473975319
AR	55.412469	22.50949525	-2.461737516
LOC100653005	8.2475975	3.350998508	-2.461235807
HOXB4	105.34739	43.27851816	-2.434172848
ADAMTS18	434.70468	179.1417361	-2.426596316

Supplementary table 4

Gene	Control	miR-1972	Fold change
NA	13.477512	5.73097703	-2.351695341
WNT7A	15.447567	6.5959604	-2.341973866
MYZAP	33.903223	14.4923365	-2.339389707
OR56B4	9.7229856	4.19337858	-2.318651993
OR9A2	8.0653226	3.48323729	-2.315467465
LOC101927787	7.9913701	3.45831331	-2.310771005
CHGB	8.1681129	3.54332916	-2.305208606
KRTAP20-2	29.285164	12.7081072	-2.304447358
PRAP1	33.56208	14.5760592	-2.302548266
NA	100.72619	43.896318	-2.294638731
SNORD116-23	16.303739	7.1392755	-2.283668505
MRGPRD	23.46354	10.2975709	-2.278550903
OTX2-AS1	9.2428404	4.06542234	-2.273525255
VCX2	24.73997	10.8904474	-2.271712887
CCL20	550.19478	243.761831	-2.257099817
HERC5	54.595001	24.3127344	-2.245531103
NUDT6	30.722716	13.70904	-2.241055275
MIR486-1	26.263357	11.7336137	-2.238300767
PPP1R2	18.843284	8.47145656	-2.224326393
KLRC4	7.2162493	3.25578343	-2.21644021
WASH2P	48.972445	22.1530804	-2.210638155
LOC101929432	13.784772	6.25262569	-2.204637308
MT1DP	11.026036	5.00357406	-2.203632098
LOC146880	66.648582	30.2481215	-2.203395757
MEIS3P1	35.028675	15.9062215	-2.202199599
MPV17L	20.474956	9.30900528	-2.199478415
FAM90A10P	45.71649	20.8937526	-2.188045906
LINC01194	12.772876	5.83887873	-2.187556361

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
LOC101927093	12.016116	4.982594548	-2.411618252
WASH2P	48.972445	20.55269743	-2.382774566
FAM86C1	71.744202	30.31385909	-2.366712928
MFI2	32.289194	13.65048454	-2.365424773
GTF2H2C	31.198201	13.21211303	-2.361333219
TCEB3C	20.505798	8.691924948	-2.359177942
ULBP1	138.74051	59.33106971	-2.338412419
SEMA3C	17.762638	7.615096925	-2.332555725
OR52B2	10.268392	4.432985624	-2.316360322
LOC392196	8.4948031	3.681833929	-2.307220609
MS4A6A	8.0245038	3.47994983	-2.30592515
MIR3922	12.334941	5.349264878	-2.305913318
OR1I1	16.742456	7.293838349	-2.295424664
OR9A2	8.0653226	3.531263202	-2.283976625
BCRP3	5.6755798	2.490815925	-2.278602672
ATAD3B	20.682	9.079103596	-2.277978153
MPV17L	20.474956	8.992153076	-2.276980387
SCARNA20	32.691326	14.36285606	-2.276102014
SNORA37	70.881215	31.16321208	-2.2745157
DKFZp779M0652	20.45614	8.993667459	-2.274504843
LTB4R	15.754141	6.938430161	-2.270562674
MCTP2	20.801869	9.170499711	-2.26834625
GOLGA6A	25.396446	11.21270782	-2.264969885
PTTG1	50.47561	22.44730792	-2.248626434
RAG1	7.3748208	3.280277804	-2.248230555
MAL2	200.09982	89.18767198	-2.243581587
MC5R	59.506186	26.69199241	-2.22936472
C8orf88	26.138486	11.75296048	-2.223991677

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
MIR222	30.777858	12.71403111	-2.420778916
SPX	53.909972	22.28490621	-2.41912492
ART4	181.22422	75.26874347	-2.407695623
NA	19.527281	8.110974246	-2.407513622
SNAP29	709.03274	295.3831966	-2.400382782
LOC101927614	28.168854	11.7726251	-2.392741995
MIR4778	17.514362	7.328019487	-2.390053987
INHBA	198.31501	83.17164041	-2.384406562
MBL1P	20.287732	8.508703231	-2.384350636
MARCH4	130.2773	55.04379546	-2.366793606
SNORD114-17	17.246776	7.305854876	-2.360678707
PSG4	11.156337	4.746644615	-2.35036285
TNFRSF10C	1118.0527	475.8910307	-2.349388044
RSPH10B	7.4606891	3.177986958	-2.347614764
IGHV3-15	20.674388	8.812356875	-2.346067918
MAGEA4	10.062814	4.2910535	-2.345068442
SPATA31C1	15.987191	6.855096433	-2.332161369
NEIL1	55.108704	23.66023875	-2.329169396
LOC101927762	22.714008	9.77657232	-2.32330995
PLAC8	127.6167	55.19549704	-2.312085389
APOB	15.872648	6.872589606	-2.30955853
SRD5A3	239.66342	103.9993315	-2.304470737
LOC101927963	28.95375	12.5833578	-2.300955793
LOC728739	12.868266	5.593566117	-2.300547692
KCNIP3	68.335323	29.7675687	-2.295629983
BVES	176.25385	77.03322443	-2.288023812
MIR635	13.630017	5.971990277	-2.282324127
APOC4-APOC2	7.9134985	3.470484769	-2.280228551

Supplementary table 4

Gene	Control	miR-1972	Fold change
TMEM120B	40.896928	18.7024388	-2.186716307
SPIN2B	122.95207	56.2344589	-2.186418619
MORN4	56.727548	25.9538053	-2.185712154
LOC100653133	21.809327	9.99432321	-2.182171471
CCDC144CP	12.791317	5.86362469	-2.181469254
IFI44	133.41588	61.2161764	-2.179421934
LOC101927476	26.184076	12.0161407	-2.179075374
NA	23.946665	10.992191	-2.178516046
SNORA31	8.2621694	3.79922543	-2.174698393
OR11H4	7.6838275	3.54096059	-2.169983911
LOC100499484	5.0876713	2.34969305	-2.165249343
WNT5A	16.249095	7.51389847	-2.162538528
FAM24B	15.749133	7.28712969	-2.161225844
IL23A	13.682207	6.34478798	-2.156448298
PARP9	139.17353	64.6018083	-2.154328677
LOC101928208	7.5076719	3.49124833	-2.150426206
GAL3ST4	27.671338	12.9157916	-2.142442282
GPM6A	12.320204	5.75809051	-2.139633549
SNORA14A	8.7032152	4.07995563	-2.133164172
LOC100132077	15.376462	7.23064779	-2.126567702
LOC101805491	9.9547948	4.7102028	-2.113453534
LOC101928758	14.345728	6.79132824	-2.112359701
ANKRD20A19P	20.000796	9.48037042	-2.109706125
NA	19.527281	9.27122546	-2.106224368
LGALS2	11.306289	5.38049408	-2.101347697
SNTA1	26.647823	12.6826642	-2.101121854
LOC648691	8.1109742	3.8611913	-2.10064035
FAHD2CP	36.300657	17.3065321	-2.097511883

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
ATF3	119.71539	53.83813817	-2.22361675
LOC100499484	5.0876713	2.292114628	-2.219640885
ZRSR2	48.892934	22.02924829	-2.219455404
NA	23.946665	10.82826084	-2.21149683
OAS3	143.5634	65.00314073	-2.208560999
NA	13.477512	6.13233477	-2.19777825
ISG15	86.138685	39.21879092	-2.19636258
PHOSPHO2	10.563336	4.810446588	-2.195915958
FAP	24.910904	11.38944806	-2.187191463
MIR4421	7.1796704	3.295669203	-2.178516695
CRHR1-IT1	20.089424	9.241534006	-2.173819199
LOC101929224	10.432801	4.830613552	-2.15972591
WNK3	13.693084	6.35384315	-2.155086943
LOC101929018	15.302488	7.104013479	-2.154062345
KRT7	157.59504	73.17646006	-2.153630266
MIR103A2	15.848983	7.371462432	-2.15004592
SNORD90	13.086034	6.089325173	-2.149012233
CSF3	231.59642	107.7857809	-2.148673181
MIR4691	17.690165	8.236357638	-2.147814135
HMGN3-AS1	27.493646	12.83082317	-2.142781123
BHLHA15	33.310407	15.57093173	-2.139268727
LOC101927787	7.9913701	3.740624581	-2.136373208
MIRLET7D	30.336448	14.20402136	-2.135764708
NUPR1	256.21149	120.4115772	-2.127797781
FAM106B	45.828554	21.54747363	-2.126864352
FAHD2CP	36.300657	17.12179759	-2.120142849
BHLHB9	80.141889	37.94302461	-2.112163968
TNFRSF9	257.13256	122.0000847	-2.107642481

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
TNFSF10	557.85291	244.910234	-2.277785195
ELFN1	18.797539	8.290007295	-2.267493711
PCDHB14	14.096632	6.216949227	-2.267451635
WNT4	16.200032	7.203803003	-2.24881658
OR1L8	15.80286	7.030291468	-2.247824256
MIR99B	38.934152	17.35779107	-2.243036094
FAM90A25P	18.293829	8.18466969	-2.23513349
ARHGEF9	66.718517	29.88183714	-2.232744811
CCDC170	12.507065	5.605656207	-2.231150879
FOXN3	267.67543	120.7219284	-2.217289194
SPATA31D4	52.537002	23.77881235	-2.209403945
SSR4P1	15.9149	7.227865271	-2.201881152
RPP21	65.510013	29.8588172	-2.193992216
SNORD116-23	16.303739	7.472983552	-2.181690685
EOGT	1182.6323	543.6556148	-2.175333613
ZRANB3	41.99037	19.35195525	-2.169825727
KRT8	94.071317	43.38959574	-2.16806162
CSF2RB	181.21089	83.66057466	-2.166024969
ZNF135	43.033387	19.89423413	-2.163108504
PRKCQ-AS1	18.682672	8.637431222	-2.162989379
FBXL20	169.44632	78.63957116	-2.154720769
FAM183CP	9.659383	4.483245283	-2.154551529
LIMD1	120.04327	55.8711176	-2.148574652
KCNK15	8.1159598	3.782414389	-2.145708798
LOC100505767	14.36804	6.71036365	-2.141171644
C15orf41	160.87271	75.19278445	-2.139470081
LINC00968	5.7392353	2.684156344	-2.138189644
NCDN	61.103322	28.60006544	-2.136474895

Supplementary table 4

Gene	Control	miR-1972	Fold change
SPX	53.909972	25.7059981	-2.09717482
LOC100507033	7.975731	3.8099579	-2.093390841
PRICKLE2-AS3	8.5089313	4.07272833	-2.089245979
RASD1	34.696317	16.6503001	-2.083825336
LOC101927307	11.172323	5.37029784	-2.080391755
LINC00314	7.2696764	3.50126947	-2.076297304
KIR3DL3	10.644604	5.12673268	-2.076294016
LTB4R	15.754141	7.59882365	-2.07323413
URAHP	24.201609	11.6736665	-2.073179785
TNC	58.996173	28.48733	-2.070961812
BEAN1	16.271324	7.86168148	-2.069700184
OR4D5	12.497601	6.04888012	-2.066101657
MIR4655	13.114765	6.35305261	-2.064324892
KCNK15	8.1159598	3.93897205	-2.060425851
LOC101929128	59.847605	29.0713246	-2.058647355
NA	13.635816	6.64484074	-2.052090767
ISM1	13.625324	6.65669694	-2.046859564
TRAV8-4	9.7831196	4.78080476	-2.046333229
MIR4766	6.6366593	3.24326777	-2.046287814
MIR1236	9.1810725	4.49104638	-2.044305886
CMPK2	21.920706	10.7273069	-2.04344909
MIR3620	18.914185	9.27596693	-2.039052642
TRIM61	10.564267	5.22672983	-2.021200055
C1orf56	32.546316	16.2239558	-2.00606538
NDNF	6.7388105	3.36171983	-2.004572323
LENG9	36.130355	18.0370361	-2.003120412
FAM184A	23.698537	11.8357157	-2.002290184
SNORD90	13.086034	6.53663591	-2.001952452

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
LOC101929236	27.750622	13.2206688	-2.099033161
TCF7	15.881922	7.57254749	-2.097302401
LINC00520	94.107114	44.94599662	-2.093781894
XAF1	278.50109	133.0669731	-2.092939205
KCNG1	39.316069	18.79975779	-2.091307219
CLDN4	8.3219056	3.984351073	-2.088647675
AQP12B	16.478113	7.902736018	-2.08511491
FUK	23.044978	11.06946454	-2.081851159
ACSL5	46.477792	22.34686234	-2.079835256
TCEB1	17.570283	8.471456565	-2.074056878
TRAJ59	12.598117	6.08730084	-2.069573648
MIR519A1	7.9139383	3.828504813	-2.067109411
IGHV1-2	14.146971	6.852068907	-2.064627703
RRN3P3	48.374306	23.47948573	-2.060279627
FBXO4	19.426092	9.443845215	-2.057010793
SEC14L1P1	34.924125	17.00567329	-2.053674946
CD69	29.630785	14.44838181	-2.050802988
NSUN5	71.939982	35.16759761	-2.045632529
IGHV1-58	8.0111623	3.917879294	-2.044770066
BIRC3	444.32443	218.3262653	-2.035139587
ZNF571-AS1	19.890106	9.794031025	-2.030839643
PPP3CB-AS1	27.810221	13.69887966	-2.030109169
LOC400743	26.780546	13.195121	-2.029579453
IGHJ2	17.117605	8.462056752	-2.022865738
ZNF594	24.824052	12.27555396	-2.022234731
GATM	12.987931	6.427932114	-2.020545807
FOS	36.085853	17.87232121	-2.019091581
SNORD116-23	16.303739	8.077362048	-2.018448413

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
THAP3	32.610594	15.26622004	-2.136127598
LOC101928758	14.345728	6.721165165	-2.134410887
SLC46A1	32.538247	15.25109587	-2.133502227
LOC101929295	10.141599	4.757493376	-2.131710667
CYP4V2	55.975956	26.26421885	-2.13126294
HIST1H2BE	22.4107	10.54582793	-2.125077348
IGHV3-16	24.882514	11.71450997	-2.124076371
OR9A2	8.0653226	3.798950104	-2.12303989
MIR4421	7.1796704	3.388884712	-2.118593871
RAB3B	341.44394	161.6020153	-2.112869315
C15orf57	60.485308	28.82517649	-2.098349958
LOC391322	15.791748	7.526398724	-2.098181202
HNF4A	14.313027	6.824117665	-2.097417978
LOC100288814	8.2888215	3.964398532	-2.090814389
LOC100379224	67.265598	32.27005962	-2.084458439
LINC00265	87.955491	42.34777111	-2.076980421
MIR103A2	15.848983	7.648810955	-2.072084513
UBA7	55.463365	26.77271235	-2.071637883
MAPK8IP1	8.6663537	4.183652986	-2.071480042
ZNF816	22.672142	10.976142	-2.065583893
SYNPO	227.79118	110.3204067	-2.064814534
LOC101928323	55.989253	27.12333933	-2.064246309
MIR105-1	8.827525	4.279532776	-2.062731012
NA	9.9308643	4.815821867	-2.062132811
MIR3939	21.431411	10.40480975	-2.059760043
ZNF826P	11.24268	5.464149113	-2.057535353
POP5	71.108726	34.64638723	-2.05241387
IFNA4	6.7784289	3.302769798	-2.05234675

Supplementary table 4

Gene	Control	miR-1972	Fold change
BIRC3	444.32443	222.02669	-2.001220779
TRBJ2-6	43.896318	21.9796293	-1.997136416
HOXB-AS1	52.908532	26.5293663	-1.99433834
RNF207	29.201578	14.6559018	-1.992479101
DPY19L2P3	6.9522645	3.49000333	-1.99205098
FGFR2	8.3530441	4.20697833	-1.985521067
SKP1	17.720618	8.95072008	-1.97979808
CRHR1-IT1	20.089424	10.1482559	-1.979593766
FLJ13224	19.363927	9.79080216	-1.977767184
LOC391322	15.791748	7.99218757	-1.975898112
ZNF774	44.77574	22.6956726	-1.972875659
C19orf44	41.826858	21.2181981	-1.971272873
NA	15.617896	7.93620622	-1.967929742
IRAK2	399.68252	203.1746	-1.967187419
CASC1	7.4049598	3.7706284	-1.963852981
MIR4532	8.2429232	4.19856437	-1.963271832
TSACC	12.236244	6.23602582	-1.962186308
MYHAS	13.270634	6.77113413	-1.959883557
IDO1	7.6409024	3.9046947	-1.956850138
LOC101928800	5.2658414	2.69916935	-1.950911827
ZNF140	55.718749	28.6023686	-1.948046689
MTRNR2L2	14.850906	7.63831935	-1.944263516
CNR1	20.289823	10.4393769	-1.943585674
LINC00702	36.317201	18.688022	-1.943341092
ZNF322	35.645737	18.3900592	-1.938315536
NTNG2	18.045358	9.31296135	-1.937660569
LINC00906	5.9607095	3.07748899	-1.936874339
MDGA1	18.568745	9.60420722	-1.933397005

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
G0S2	25.557311	12.66451248	-2.01802564
PPIAL4C	9.0359666	4.477907614	-2.017899289
LOC101060400	8.6568048	4.296303749	-2.014942452
BOP1	537.44534	266.772529	-2.014620268
SLC10A5	14.215453	7.065516628	-2.011948085
POMZP3	73.756933	36.70048366	-2.009699221
ZNF540	6.1819329	3.077381727	-2.008828762
ZNF561	71.928955	35.8278012	-2.00762961
AFF3	66.179731	33.01176564	-2.004731643
LOC101928126	6.922708	3.454421236	-2.004013857
ANKRD20A19P	20.000796	9.994907009	-2.001098713
PCDHA6	10.661301	5.331118885	-1.99982432
CIR1	83.639268	41.91981535	-1.995220323
HIF1A-AS2	72.609086	36.42915489	-1.993158679
MIR99B	38.934152	19.54327805	-1.992201706
FHL1	10.532043	5.294150286	-1.989373553
BCL2A1	135.68444	68.34073181	-1.985410929
MSC	118.64386	59.94277936	-1.979285213
LOC101928595	8.7097008	4.404105756	-1.977632085
SCARNA5	73.963345	37.40252924	-1.977495821
SLC12A7	447.34108	226.653451	-1.973678659
CCNT2-AS1	27.436378	13.91017789	-1.972395896
ZNF667	37.301925	18.91210769	-1.972383275
RPP21	65.510013	33.21706702	-1.972179316
LPAL2	7.2598486	3.692447558	-1.966134518
FAM226A	4.3046828	2.190131544	-1.965490525
OR2B11	12.49946	6.372554927	-1.961451913
RGPD4-AS1	6.7100241	3.422496493	-1.960564207

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
FOSL1	1498.9588	730.4984805	-2.051967079
RNASE3	6.6439513	3.243974808	-2.048089685
TNNC1	10.773936	5.26130354	-2.047769298
C8orf88	26.138486	12.80228048	-2.041705486
PLXDC2	186.74643	91.51945584	-2.040510743
INVS	128.12996	62.87458082	-2.03786585
LGALS2	11.306289	5.554698791	-2.035445895
SLC9A9	38.729645	19.05145334	-2.032897124
FCN2	7.0788299	3.487952775	-2.02950854
MIR3134	6.1515221	3.034256748	-2.027357142
ZBTB16	6.9431067	3.42915235	-2.024729727
CMA1	10.484304	5.187244078	-2.021170289
NA	13.477512	6.673153082	-2.019661742
TECPR2	53.195373	26.34241221	-2.019381255
LOC101927881	9.2529391	4.587866547	-2.016828301
UGT1A10	17.01861	8.445339053	-2.015148224
LOC101929187	6.2764561	3.117437405	-2.013338287
OR1B1	7.4548818	3.704677695	-2.012288897
C11orf96	35.819422	17.80951824	-2.011251577
LOC101805491	9.9547948	4.96609919	-2.004550125
MAP7D1	247.84328	123.8010358	-2.001948368
BCRP3	5.6755798	2.835744829	-2.00144236
ADAM28	8.4714608	4.23790071	-1.998975755
FBXL14	59.47654	29.80801461	-1.995320422
LOC101929356	13.179781	6.612532414	-1.993151773
MIR539	20.944025	10.51977999	-1.99091855
C8orf31	12.22449	6.16185356	-1.983898236
KRT7	157.59504	79.44563235	-1.983684118

Supplementary table 4

Gene	Control	miR-1972	Fold change
LOC101929356	13.179781	6.82009677	-1.932491744
LOC100507373	26.924937	13.952683	-1.929731865
KCNG1	39.316069	20.3870765	-1.928479994
FAM46C	18.232446	9.46034117	-1.927250366
LOC100132731	10.057052	5.23097066	-1.922597684
KRTAP1-5	9.8503901	5.12473535	-1.922126585
ULBP1	138.74051	72.2086302	-1.921384049
ZNF17	10.735423	5.58879789	-1.920882339
AADACP1	22.855167	11.899648	-1.920659075
HIST1H2BE	22.4107	11.6783169	-1.919000847
GGTLC1	10.499565	5.47410432	-1.918042475
PTCHD1	7.7425401	4.04569639	-1.913771908
SUGT1P3	5.5935661	2.92561512	-1.911928222
DLX2	22.947021	12.0155573	-1.909775832
OAS3	143.5634	75.3454185	-1.9054032
LOC101928227	5.8825058	3.08935408	-1.904121594
TRAV38-1	32.499471	17.0913157	-1.901519543
NA	15.493125	8.14932862	-1.901153604
LOC101927617	5.077336	2.67472753	-1.898262888
GPNMB	12.868266	6.78688655	-1.896048434
LOC100134368	12.110026	6.38823628	-1.895675921
ARHGEF25	34.176077	18.0579624	-1.892576595
IFIT5	83.269499	44.0047661	-1.892283642
MIR1296	11.267197	5.95793532	-1.891124464
LOC101927318	13.137545	6.95161436	-1.88985523
ZNF30	24.107179	12.764887	-1.888554043
MIR3675	5.9886268	3.17491528	-1.886231999
LOC101927676	5.6647494	3.00704753	-1.883824372

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
PCOLCE-AS1	11.41161	5.824840749	-1.959128308
AHRR	61.652453	31.48904178	-1.957901834
NA	11.182511	5.715979183	-1.956359588
MIR4674HG	17.479948	8.953300746	-1.952346764
SIX1	12.039749	6.179216302	-1.948426598
CXCL5	175.23017	90.03911249	-1.946156122
PSMB8-AS1	17.871672	9.183944036	-1.94596913
MT1DP	11.026036	5.667546052	-1.945469221
LILRA6	6.6836709	3.436215452	-1.945067474
IL6	236.85212	121.7802056	-1.944914771
HERC5	54.595001	28.09146887	-1.943472644
WNT5A	16.249095	8.373526989	-1.940531746
LOC101927881	9.2529391	4.76985743	-1.939877497
OR5M10	10.777497	5.556372013	-1.939664374
C11orf96	35.819422	18.4734293	-1.938969808
LOC283683	5.9040635	3.04513397	-1.938851792
LOC101927685	13.020529	6.715654968	-1.938832355
NNT-AS1	94.813182	48.92289711	-1.938012415
OR52N2	7.1830612	3.708603554	-1.936864131
NA	12.364946	6.384264946	-1.936784595
CBX8	26.661145	13.77173435	-1.935932297
FAM69C	8.4916604	4.393342789	-1.932847213
CCL18	19.072468	9.870641571	-1.932241993
DLX2	22.947021	11.88017747	-1.931538565
SSR4P1	15.9149	8.252688715	-1.928450334
SNHG7	57.041024	29.62115147	-1.925685564
MIR2861	11.204021	5.819429362	-1.925278282
TCF15	13.881516	7.213061679	-1.924497065

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
OLFML2A	9.0526005	4.572023741	-1.979998583
FHL1	10.532043	5.326488373	-1.977295702
CYP2S1	45.632817	23.0788406	-1.977257753
C5orf56	25.252187	12.77600175	-1.976532817
REG1A	7.1451142	3.615908931	-1.976021605
LOC101929637	6.4286302	3.254265263	-1.975447515
RUNX1T1	262.91543	133.2095742	-1.973697723
LOC101928548	8.2900073	4.200715973	-1.973474843
PURA	178.2647	90.52889844	-1.969146877
OR2A12	4.3721576	2.221454367	-1.968150996
MIR4717	9.3590275	4.757493376	-1.967218189
RGPD4	8.8829211	4.525452832	-1.962880047
IQCG	22.797354	11.61658481	-1.962483341
POM121L10P	22.869521	11.65604624	-1.962030777
SNORD116-26	24.756867	12.62236863	-1.961348777
POU2F1	194.73156	99.29722427	-1.961097733
LINC00202-1	7.6694861	3.915180538	-1.958909956
GRM2	7.6544346	3.911442022	-1.956934187
SPATA24	18.067345	9.260520659	-1.95100746
TENC1	137.34608	70.61756154	-1.944928047
SLC40A1	157.61093	81.20832284	-1.940822397
PCDHA6	10.661301	5.494497966	-1.940359477
MIR1290	4.6830927	2.415843801	-1.93849149
OR2Y1	7.729245	3.988034249	-1.938108979
ZNF707	27.110236	13.99170329	-1.937593666
NLK	289.92268	149.6889423	-1.936834335
TEAD1	187.18104	96.64703224	-1.936748944
ASNA1	309.68768	159.9317588	-1.936373851

Supplementary table 4

Gene	Control	miR-1972	Fold change
IGLL3P	11.004432	5.84669487	-1.882162855
OR3A2	8.3961204	4.46139367	-1.881950136
TMEM52	17.949784	9.55682439	-1.878216376
FOLR3	12.056291	6.42906001	-1.875280591
NUPR1	256.21149	136.84608	-1.872260332
CYB561D1	30.52403	16.3150016	-1.87091797
MIR593	39.96878	21.3636283	-1.870879782
TRBV27	9.279098	4.96276208	-1.869744676
MYH1	7.7542564	4.14912051	-1.86889158
LOC100507191	4.8699013	2.60794233	-1.867334741
HERC6	143.12542	76.6595904	-1.867025608
SLC46A1	32.538247	17.4368454	-1.866062714
CD164L2	14.386944	7.72502425	-1.862381735
SMARCD3	36.227587	19.4614793	-1.861502203
AGMAT	16.41605	8.81961055	-1.861312336
LOC101927685	13.020529	6.99782848	-1.860652798
CLEC18C	24.896504	13.3841814	-1.860143924
NA	34.806005	18.711929	-1.860097079
FDPSP2	11.420594	6.14253669	-1.859263499
OR5AR1	12.000451	6.46691368	-1.855668917
SUMO1	8.2937031	4.47134789	-1.854855246
ATG10	30.533421	16.4843338	-1.852269059
SSBP2	143.99452	77.8049216	-1.850712175
SOWAHC	18.856718	10.191137	-1.850305644
AJUBA	94.311506	51.0580424	-1.847143013
NA	121.65274	65.9588161	-1.844374212
SPATA3-AS1	8.4756234	4.5962336	-1.844036691
LOC101060153	11.987916	6.5106873	-1.841267364

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
IGKV3-11	12.5196	6.507798904	-1.923784116
LOC642441	38.897501	20.22087903	-1.923630565
ZDHHC11	9.1561359	4.760522714	-1.923346757
RCSD1	17.906593	9.34091215	-1.917006934
LOC101928219	12.797946	6.683993916	-1.914715424
ARPIN	58.985348	30.86451275	-1.911105768
FAM205A	8.6669624	4.535934044	-1.910733779
MYH6	7.5979304	3.977267202	-1.910339445
LAMC2	245.05584	128.3521686	-1.909245844
CFL1P1	7.6705451	4.021498432	-1.907384818
LOC728739	12.868266	6.74660733	-1.907368399
ASB16	19.519411	10.24665684	-1.904954115
PI3	24.05144	12.64867949	-1.901498109
GPR135	24.556708	12.91556244	-1.901327046
LGALS2	11.306289	5.951453434	-1.899752553
LURAP1L-AS1	197.06642	103.7855616	-1.898784507
FOXF1	213.31025	112.7329128	-1.89217369
HMSD	8.04396	4.252003265	-1.891804758
MIR1238	22.187246	11.72903106	-1.891652098
TAS2R4	12.403021	6.559160335	-1.890946524
TRAJ58	5.6882874	3.009111943	-1.890354189
EPHB3	13.844984	7.326665646	-1.889670514
CTD-2337A12.1	23.980523	12.7024499	-1.887865983
LOC101928917	8.5080213	4.512383059	-1.885482941
CYP2D7P	16.948262	8.991055384	-1.885013654
TNC	58.996173	31.30294242	-1.884684572
IGHV3-15	20.674388	10.98236654	-1.882507533
CDCP2	7.3877689	3.927751972	-1.880915321

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
LOC101928117	9.8939649	5.109866018	-1.936247423
KIF9-AS1	9.0359666	4.672331361	-1.933931027
LINC00997	26.093375	13.50595871	-1.931989869
ARL11	8.7718139	4.540811967	-1.931772103
ZNF525	17.375198	9.02259898	-1.925742004
MXD3	11.896776	6.197842392	-1.919502775
ADAM19	140.32055	73.13233369	-1.91872111
IL3RA	68.483305	35.7058074	-1.917987855
AQP12A	14.345191	7.489275027	-1.915431258
ZNF134	278.00817	145.2108416	-1.914513856
MYL10	10.777894	5.635658463	-1.912446272
CDON	19.351556	10.13577276	-1.909233406
TTTY20	11.532613	6.04298735	-1.908429041
KLRC4	7.2162493	3.784102294	-1.906991077
ZNF709	31.16079	16.366191	-1.903973281
IL33	10.022993	5.27326071	-1.900720081
FAM111B	183.34957	96.49773333	-1.900040186
MIR574	94.941875	49.99631646	-1.898977402
OTX2-AS1	9.2428404	4.876291049	-1.895465278
TUBA4A	21.496473	11.35223142	-1.89359012
CDCP2	7.3877689	3.904084133	-1.892318047
MIR4500HG	7.6862242	4.062739123	-1.891882299
HNRNPA1L2	9.7129412	5.137439173	-1.890619213
POM121L8P	69.141378	36.61612453	-1.888276799
LOC101928923	6.8081471	3.606499323	-1.887743907
MIR32	12.805488	6.78691594	-1.886790383
LOC101927787	7.9913701	4.237186214	-1.886008717
MAF	35.989853	19.10596072	-1.883697653

Supplementary table 4

Gene	Control	miR-1972	Fold change
LINC01491	8.4059163	4.56629039	-1.840863276
MAFA	18.810741	10.2369497	-1.837533766
LOC101928796	10.0652	5.48034427	-1.836599867
NPIPB6	70.754882	38.5412708	-1.835821197
LOC283070	30.162809	16.433859	-1.835406318
LOC101929715	11.456978	6.24282024	-1.835224733
LOC390937	11.762824	6.41877336	-1.832565763
MC5R	59.506186	32.5022919	-1.830830466
TTLL3	15.637419	8.54816113	-1.829331376
ST7-OT4	10.542052	5.76734333	-1.82788704
KRTAP19-5	24.896504	13.6205338	-1.82786549
FAM205A	8.6669624	4.75048058	-1.824439077
MIR524	5.5958141	3.07679863	-1.818713137
CTC-338M12.4	37.366622	20.5938454	-1.814455773
LOC100996713	11.926805	6.57711248	-1.813380051
DUSP2	26.899397	14.8389196	-1.812759806
NDUFB9	161.00095	88.829287	-1.81247604
PLAC8	127.6167	70.4779659	-1.810731917
FLCN	177.78955	98.23397	-1.80985817
CECR2	28.51924	15.7666223	-1.808836384
IFIH1	117.03465	64.7110649	-1.808572539
LOC101929125	12.260144	6.7790903	-1.80852347
BRSK1	12.424559	6.87478222	-1.807265858
HOXB9	96.074611	53.167437	-1.807019793
UNCX	15.720183	8.70789206	-1.805279963
LOC283278	6.7006213	3.71296661	-1.804654349
SLC38A5	21.147007	11.7212963	-1.804152575
IGLV1-36	60.171316	33.3867506	-1.802251329

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
PDYN	7.7628947	4.127836988	-1.880620463
RRAD	24.935128	13.27856604	-1.877847939
FBF1	35.135003	18.71727328	-1.877143216
UTS2	6.8898436	3.671248463	-1.876703164
LOC101928208	7.5076719	4.002797968	-1.875606003
LOC101927759	14.263708	7.605978569	-1.875328452
TCEB3CL2	15.498478	8.308153557	-1.865453978
PRR4	34.046316	18.26278007	-1.864246061
LINC01097	9.0382227	4.849058941	-1.863912731
LOC100506753	20.704179	11.1116432	-1.863286845
MIR151A	8.4684755	4.548786216	-1.861700037
RGPD4	8.8829211	4.772284834	-1.861356012
IDO1	7.6409024	4.107818395	-1.860087674
LOC286297	18.557671	9.976954577	-1.860053701
CXCL12	9.2597031	4.979083719	-1.859720299
RNASE3	6.6439513	3.574223396	-1.85885173
MIR1296	11.267197	6.063173509	-1.858300314
MIR4451	5.6808649	3.057432883	-1.858050551
IFIH1	117.03465	63.12842467	-1.853913756
LOC391322	15.791748	8.526591864	-1.852058663
PPIP5K1	31.090369	16.79737333	-1.850906605
KIF27	34.246602	18.50759133	-1.850408361
ZNF322	35.645737	19.28920054	-1.847963439
IFNA4	6.7784289	3.670366856	-1.846798733
SNAPC1	529.56051	286.9654263	-1.845380879
PRAMEF25	17.980091	9.74557507	-1.844949173
SNORA80A	55.246316	29.96118282	-1.843929754
AWAT2	8.6892611	4.71422607	-1.843199924

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
ZNF860	27.446344	14.58819571	-1.881407689
ACCS	22.472411	11.95897609	-1.879124977
PIK3C2B	140.87825	75.00386114	-1.878280032
MGRN1	886.03432	471.9657396	-1.877327627
TMEM176B	15.360378	8.214402309	-1.869932578
MIR4793	10.168901	5.440508378	-1.86910861
AKR7A2	41.303951	22.10361154	-1.868651688
OR2B11	12.49946	6.690115175	-1.868347513
BCL7B	308.62994	165.2285794	-1.86789684
IGHV1-58	8.0111623	4.29016125	-1.867333612
TAS2R9	5.4146905	2.901022105	-1.866476808
HOXB-AS1	52.908532	28.37009542	-1.86494023
WNK3	13.693084	7.343879894	-1.864557238
LOC284632	11.825297	6.347225219	-1.863065564
GDPD1	43.552197	23.39532333	-1.861577049
NA	11.182511	6.011274966	-1.860256059
LINC00278	10.329464	5.554209423	-1.859754196
S100A2	25.760926	13.85328546	-1.859553543
PKNOX2	21.101446	11.36013671	-1.857499265
MIR139	15.672838	8.438073258	-1.857395351
PBLD	36.659114	19.73716016	-1.857365198
CIB2	39.897261	21.48408078	-1.857061573
MIR500A	12.095387	6.514714732	-1.856625705
LOC283070	30.162809	16.26275013	-1.854717586
EHD2	1806.1213	974.0958657	-1.85415153
UQCC3	80.083816	43.2163498	-1.853090703
TRIM61	10.564267	5.703137641	-1.852360452
HOXA-AS2	13.514191	7.30518015	-1.849946289

Supplementary table 4

Gene	Control	miR-1972	Fold change
LOC101929709	30.700212	17.0663779	-1.798870961
SNORD111	72.030327	40.1018619	-1.796184097
FAM215A	26.465601	14.7353617	-1.796060479
LOC100130899	8.1781793	4.55468446	-1.795553423
MIR4663	12.367659	6.89694648	-1.79320786
BHLHE40-AS1	7.8336264	4.36869984	-1.793125333
ICAM4	10.148237	5.67035666	-1.789699985
FSTL5	13.349232	7.46157872	-1.789062627
USP27X	39.179744	21.9050443	-1.788617426
PMEL	10.094079	5.64398218	-1.788467588
LINC00937	14.096305	7.88438382	-1.787876556
HIST3H2BB	87.460429	48.9581422	-1.786432757
LOC101928595	8.7097008	4.88048057	-1.784599021
MIR4520-2	4.984266	2.7930445	-1.784527958
PLCE1-AS2	18.655915	10.462838	-1.783064534
NA	8.2091373	4.60445122	-1.782869849
LINC00942	7.5652236	4.24583979	-1.78179677
SLC15A3	32.001739	17.9715694	-1.780686969
ZNF836	57.583461	32.3710829	-1.778854954
LILRA6	6.6836709	3.75827022	-1.778390195
BHLHA15	33.310407	18.7321139	-1.778251374
FAM86C1	71.744202	40.360381	-1.777589814
RTN4RL1	10.589059	5.95829666	-1.777195642
TAC1	8.3454718	4.70044891	-1.775462721
SNORD115-2	5.6093418	3.16144916	-1.774294497
GUSBP1	15.816466	8.91598706	-1.773944443
OR52B2	10.268392	5.79318235	-1.772495908
MIR1185-2	8.6446336	4.88830077	-1.768433244

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
CLK2	23.902474	12.98446783	-1.840851244
SLC23A3	17.222448	9.356099673	-1.840772168
CKLF	64.724861	35.18351272	-1.839636111
LOC101929453	6.3219487	3.438264999	-1.838703168
SLC6A9	200.60425	109.1182998	-1.838410714
SFTA1P	19.49458	10.60735593	-1.8378359
DDIT4	746.55359	406.3861528	-1.837054685
KRTAP5-2	13.336989	7.26434906	-1.835950958
LINC00899	32.677301	17.80452346	-1.835337042
SH2D6	13.544248	7.384436578	-1.834161348
CMA1	10.484304	5.720318831	-1.832818051
OR2T11	5.730977	3.127029783	-1.83272224
OR1B1	7.4548818	4.069346713	-1.831960341
SPATA24	18.067345	9.870387963	-1.830459447
IPO5P1	24.559373	13.41806811	-1.830321079
RGPD3	171.01405	93.55552072	-1.827941823
MIR3939	21.431411	11.73252876	-1.826666
KIF9-AS1	9.0359666	4.951000993	-1.825078727
PRICKLE2-AS3	8.5089313	4.664507484	-1.824186435
APTR	70.296316	38.57335415	-1.822406095
SNORD114-3	73.620186	40.43767276	-1.820584144
SKP1	17.720618	9.756691295	-1.816252856
ADM2	28.029784	15.44532234	-1.814774977
TTLL10-AS1	8.5534472	4.715711877	-1.813818876
LOC100289061	34.271702	18.90135704	-1.813187366
TNFAIP3	550.12826	303.6206977	-1.811893137
IL20RB	52.219605	28.83840441	-1.810766095
KIF1A	38.73679	21.4018687	-1.809972311

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
C8orf74	18.003256	9.732267744	-1.849852123
KAL1	51.488726	27.84815364	-1.848909863
PLBD1	11.904838	6.439003375	-1.848863395
CBLN3	40.035027	21.67091604	-1.847408158
FAM124B	906.7558	490.8287756	-1.8473974
TMEM198B	44.795716	24.26930083	-1.845776934
ALDH1A1	767.16764	415.8237686	-1.84493456
MIR4658	14.605297	7.925988567	-1.842709816
DPY19L2P3	6.9522645	3.77315932	-1.842557908
ZNF585A	36.317585	19.710554	-1.842545138
TARS2	76.384908	41.49631646	-1.840763577
LOC101927307	11.172323	6.073819278	-1.839423076
KIAA1377	66.603737	36.23337906	-1.838187281
IGLV1-36	60.171316	32.73944375	-1.837884484
ZSWIM5	21.709748	11.83400034	-1.83452319
IFFO2	122.0324	66.5720761	-1.833086864
THSD7A	29.294608	15.98743442	-1.832352033
ZNF382	30.858356	16.85353192	-1.830972633
MEIS1	62.386327	34.08055327	-1.830554985
LOC101928227	5.8825058	3.213812386	-1.830382458
CTRB1	7.7567282	4.237897294	-1.830324714
TMSB4Y	6.4359201	3.516784374	-1.830058205
LYRM7	87.571636	47.87712431	-1.829091401
RNASE4	129.6185	70.91543338	-1.827789779
FLJ44635	97.429616	53.44493765	-1.822990538
B4GALNT1	11.566087	6.347433069	-1.822167644
CDNF	12.34904	6.778110307	-1.821900183
TUB	31.412779	17.25246967	-1.820769996

Supplementary table 4

Gene	Control	miR-1972	Fold change
ZFP2	10.930867	6.18372521	-1.767683143
FAM115C	71.334332	40.359071	-1.767491918
LCP1	48.009553	27.1713493	-1.766918245
SLC13A3	9.6588367	5.46715218	-1.766703457
MIR3191	19.708338	11.1577154	-1.76634171
TOB1-AS1	7.9196131	4.48598744	-1.765411337
LOC100996348	10.441854	5.91620297	-1.764958663
KIAA1804	15.405794	8.73196361	-1.764298904
SPATA31D4	52.537002	29.7963197	-1.763204396
GOLGA8A	146.57132	83.1461323	-1.762815818
NNT-AS1	94.813182	53.8713165	-1.759993782
EBI3	22.105568	12.56566	-1.759204724
EML2	60.205322	34.2466205	-1.757993074
LOC100507642	10.042328	5.71267618	-1.757902591
PCDHGC5	7.2662213	4.13479846	-1.757333841
ZNF135	43.033387	24.4981982	-1.756593959
CSF3	231.59642	131.936573	-1.755361777
KRT14	6.480772	3.69469056	-1.754077057
CCNB3	10.959646	6.24969813	-1.753628095
RRAD	24.935128	14.2248097	-1.75293226
CBX8	26.661145	15.2168427	-1.752081286
AFF3	66.179731	37.8080712	-1.750412782
FAM86JP	10.16794	5.81071523	-1.749860258
BATF	10.986332	6.28208341	-1.74883582
NA	9.2250896	5.27504352	-1.748817731
RPS6KA1	47.796316	27.3387325	-1.748300351
MIR320D2	4.8950297	2.80257898	-1.746616158
POTEF	4.7549989	2.72383452	-1.745700377

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
RERG	8.1924957	4.530171159	-1.808429622
CCDC166	10.815661	5.983464143	-1.80759189
IGKV3-15	7.8440704	4.345254287	-1.805204006
C1orf140	9.0456887	5.014676328	-1.803842978
LOC390937	11.762824	6.521223067	-1.803775793
LOC101927257	8.9728071	4.978961039	-1.802144467
OTX2-AS1	9.2428404	5.13387162	-1.800364531
FAM86C2P	41.377083	22.99701732	-1.799236929
TESC	12.066715	6.706884188	-1.799153651
EML2	60.205322	33.48704628	-1.797868975
APOC4-APOC2	7.9134985	4.404938078	-1.796506174
OR3A2	8.3961204	4.676860546	-1.795247121
SELE	1899.9443	1058.771763	-1.79447959
LAIR2	5.8951982	3.285216616	-1.794462565
LOC100506047	14.0145	7.817404674	-1.792730533
ISM1	13.625324	7.601706158	-1.792403378
FCGR2A	7.3911952	4.124019443	-1.792230939
FGF13-AS1	5.0381385	2.812857974	-1.791110167
ZNF383	62.528599	34.91565903	-1.79084687
GCNT3	10.917253	6.101226713	-1.789353694
LOC100507144	10.020866	5.60148407	-1.788966276
HIRIP3	25.683499	14.3804016	-1.786007108
AZIN2	15.009807	8.417434218	-1.783180766
SLC46A1	32.538247	18.27214933	-1.780756407
ASIC2	7.189953	4.039360613	-1.779973035
GGT7	16.904424	9.505925453	-1.778303876
LOC283070	30.162809	16.97516579	-1.77687859
WFDC21P	7.2162493	4.064718572	-1.775337992

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
LOC101928360	9.1218145	5.010179486	-1.820656222
LINC00472	59.726735	32.84456033	-1.818466584
LOC100132731	10.057052	5.537244386	-1.81625577
KIR3DL3	10.644604	5.870523195	-1.813229253
C4orf27	118.82869	65.54071304	-1.813051536
SFTA1P	19.49458	10.75443482	-1.812701445
MKLN1-AS	13.478691	7.436891835	-1.812409116
NA	15.493125	8.555967727	-1.810797559
OR56B4	9.7229856	5.372153227	-1.80988613
CELP	8.7666139	4.847758691	-1.80838496
NACC1	319.51242	176.7270789	-1.807942603
KLRG1	95.037983	52.57856137	-1.807542473
MIR4451	5.6808649	3.144023157	-1.806877548
NRGN	161.83432	89.56877621	-1.806816261
LOC100507334	14.335607	7.935935743	-1.806416767
FGFR2	8.3530441	4.627229505	-1.805193387
HOXD1	80.457465	44.57635612	-1.804935893
MEOX2	34.218431	18.96081251	-1.804692228
MTRNR2L2	14.850906	8.241979991	-1.801861403
SOX9-AS1	8.5702118	4.756740237	-1.801698509
KIF21B	20.903314	11.60328505	-1.801499665
MIR548AB	18.273363	10.14733096	-1.800804833
GP9	10.49286	5.828670451	-1.800215041
SCARNA5	73.963345	41.09265458	-1.799916458
GALM	26.222445	14.57151148	-1.799569297
LOC100506217	14.174572	7.877565628	-1.799359436
CCNJ	236.61986	131.5083637	-1.799276155
LOC100506113	17.535078	9.745811064	-1.799242577

Supplementary table 4

Gene	Control	miR-1972	Fold change
RRNAD1	25.357458	14.5274941	-1.745480539
LOC642934	5.8932063	3.37647259	-1.745373642
DUPD1	7.988711	4.57995671	-1.744276536
FAM155B	10.825691	6.20828337	-1.743749493
MND1	26.478172	15.2182489	-1.739896105
LOC100506753	20.704179	11.9023046	-1.739510067
MESP1	47.092045	27.0727149	-1.739465183
LOC100506123	24.377362	14.0260843	-1.738001946
PDXDC2P	33.66315	19.3982529	-1.735370194
ELAVL3	19.486017	11.2293045	-1.735282658
LRRC3-AS1	7.0145211	4.04316297	-1.734909307
TSLP	8.6705621	5.00128828	-1.733665726
IGLV6-57	4.9087794	2.83153056	-1.733613446
RNASE3	6.6439513	3.83736119	-1.731385456
LOC101928322	6.7878849	3.92188545	-1.73077082
LOC400736	14.221742	8.22416126	-1.729263543
LOC101928917	8.5080213	4.92186321	-1.728617986
SLC32A1	13.883544	8.03637399	-1.727588047
CST2	10.11589	5.85964927	-1.726364354
DDIT4L	50.892764	29.4927888	-1.725600263
LOC101927372	5.658053	3.28052373	-1.724740768
LINC00520	94.107114	54.5921198	-1.723822309
TCF15	13.881516	8.05323586	-1.723719046
GRK7	8.9020853	5.16931045	-1.72210305
MTMR9LP	17.80459	10.3398024	-1.721946852
PCOLCE-AS1	11.41161	6.6284959	-1.721598771
AP1S3	18.415184	10.7055913	-1.72014635
MDFIC	46.56503	27.0931472	-1.718701403

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
WNT3	8.3200062	4.690749669	-1.773705021
HLA-G	27.671251	15.61146142	-1.772495908
NHLH2	8.2748781	4.675895567	-1.769688395
KYNU	18.572886	10.49507531	-1.769676341
ST6GALNAC2	19.208279	10.86042759	-1.768648539
ST3GAL5-AS1	10.855012	6.144015763	-1.766761809
SMARCD3	36.227587	20.50702182	-1.766594237
KRTAP19-5	24.896504	14.11271202	-1.764119016
CDNF	12.34904	7.000676534	-1.763978145
NA	6.0194912	3.413398767	-1.763489017
LPHN3-AS1	7.1244157	4.042374209	-1.762433505
BEX2	14.94441	8.480097419	-1.762292248
NA	29.788762	16.92749204	-1.759785929
LAT	25.656487	14.5976602	-1.757575291
LINC01208	6.4286302	3.659116657	-1.75688037
HTR1F	6.9598382	3.96340336	-1.756025705
WRAP53	70.136821	39.94210714	-1.755961956
ZNF558	24.188611	13.77797773	-1.755599536
CLEC18B	34.608425	19.72660302	-1.754403691
EGOT	13.366956	7.622413258	-1.75363834
MYH1	7.7542564	4.423368897	-1.753020508
LAMB3	38.860184	22.17307099	-1.752584639
VILL	13.160789	7.513763417	-1.751557507
SP140L	432.79631	247.2582647	-1.750381579
NXF3	6.3832574	3.650836213	-1.74843708
LOC101927221	12.608166	7.213260425	-1.747914988
LOC100506999	16.652735	9.52743	-1.747872739
TBC1D26	13.75616	7.878240327	-1.746095472

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
RASGEF1C	7.5489161	4.197614196	-1.798382536
C9orf16	35.309815	19.64893651	-1.797034421
KRTAP5-AS1	11.142772	6.201229314	-1.796864996
LINC01491	8.4059163	4.679483009	-1.796334396
PLA2R1	88.783173	49.44257831	-1.795682516
ZNF540	6.1819329	3.445581449	-1.794162471
LOC100996263	11.501867	6.411805565	-1.79385773
GALNT16	9.2479929	5.15731297	-1.793180475
LUM	61.760587	34.44309074	-1.793119785
ZNF561	71.928955	40.13419385	-1.79221127
PRR4	34.046316	19.0015149	-1.791768497
MPV17L	20.474956	11.42731499	-1.791755649
MIR205HG	8.057605	4.499843204	-1.790641289
ST7-OT3	26.453595	14.77591164	-1.790318993
CDKN2C	29.218446	16.33562719	-1.78863323
NUF2	145.65839	81.44200602	-1.788492117
RNF217-AS1	7.8931247	4.414272054	-1.788092037
SLC30A10	6.3791496	3.570753789	-1.786499432
BTK	11.421436	6.39540285	-1.785882171
MNT	88.704485	49.68058835	-1.785495857
DISP2	8.2575897	4.628199167	-1.784190652
SULF1	491.23332	275.5514461	-1.782728149
SULT1E1	21.684808	12.17067293	-1.781726268
ZNF204P	8.0758177	4.533561086	-1.781340877
PDYN	7.7628947	4.35850639	-1.781090588
MRGPRD	23.46354	13.18044211	-1.780178489
CCDC92	500.59194	281.2335486	-1.77998657
CFP	13.926674	7.829722621	-1.778693133

Supplementary table 4

Gene	Control	miR-1972	Fold change
MFSD4	10.80009	6.28828088	-1.717494892
RPL13A	40.346315	23.4968108	-1.717097497
LOC101927958	9.4476677	5.50600427	-1.715884563
MBL1P	20.287732	11.8343149	-1.714314015
SNORD116-13	7.0645466	4.12113984	-1.714221509
NA	12.364946	7.22023671	-1.712540253
ZNF585A	36.317585	21.224851	-1.711087884
ARAP2	11.561943	6.75727363	-1.711036669
CETP	15.266766	8.9357273	-1.708508442
PDYN	7.7628947	4.54437704	-1.708241776
CRYAA	12.109796	7.09154831	-1.7076378
ACCS	22.472411	13.1679353	-1.706600936
LOC101929767	29.364096	17.214511	-1.705775785
TUBB2A	44.062647	25.835448	-1.705511232
FAM183CP	9.659383	5.66384897	-1.705445014
C8orf74	18.003256	10.5633364	-1.704315325
MIR4717	9.3590275	5.49138083	-1.70431223
MRPL23-AS1	14.560925	8.54691939	-1.703645983
PRR34	11.827098	6.94243173	-1.70359589
CT47B1	9.932488	5.83330161	-1.702721496
TRBV4-1	7.8426232	4.60676563	-1.702414188
TAS2R4	12.403021	7.28630843	-1.702236676
TRBV4-2	5.7727271	3.39185702	-1.701937043
RGPD4-AS1	6.7100241	3.94386195	-1.701384127
RPL23AP53	69.549186	40.8862168	-1.701042348
C6orf147	9.669139	5.68635054	-1.700412054
DOK3	21.791259	12.8343838	-1.697881162
C5orf63	8.4070337	4.95331926	-1.697252542

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
TAP1	174.54908	99.99607464	-1.745559293
MIR219A2	12.300864	7.055335992	-1.743483831
LOC100507175	6.1707782	3.545049747	-1.740674647
SPATA3-AS1	8.4756234	4.871292749	-1.739912552
FLJ44511	12.115975	6.96575749	-1.739362179
NEK11	42.585154	24.48722627	-1.739076279
CCDC169	23.955826	13.80369586	-1.735464622
CD164L2	14.386944	8.290007295	-1.735456141
LOC642934	5.8932063	3.395885531	-1.735396028
SNORD115-2	5.6093418	3.233221806	-1.734907835
AP1S3	18.415184	10.62400379	-1.733356289
ZNF860	27.446344	15.84204044	-1.732500538
STAG3	7.1102213	4.109958561	-1.729998283
SULT1E1	21.684808	12.54423921	-1.728666624
MAGEA12	5.8002235	3.359509731	-1.726508927
PRKY	20.001295	11.58684723	-1.726206841
ZNF578	7.3379769	4.251781938	-1.725859186
IGLV1-36	60.171316	34.92648755	-1.722798939
ADORA1	20.282599	11.77728304	-1.722179813
TRAV13-2	14.772022	8.581337547	-1.721412536
SYP	7.4736669	4.342118705	-1.721202795
MORN4	56.727548	32.95892491	-1.721158923
KLF4	46.48123	27.03686018	-1.719180008
CXCL3	129.44355	75.29555482	-1.719139332
TARID	8.2101722	4.78100492	-1.717248224
LOC101927391	4.895287	2.850841351	-1.717137643
SUMO1	8.2937031	4.830409692	-1.716977155
BTN2A3P	24.335084	14.1784148	-1.716347321

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
ST6GALNAC4	339.90262	191.1367339	-1.778321821
LOC389705	11.593037	6.52021205	-1.778015316
CD164L2	14.386944	8.091955095	-1.777931773
UBQLN2	316.18551	177.9668888	-1.776653587
HTR2B	42.732444	24.05533109	-1.776423026
PAIP2B	17.005702	9.581171652	-1.774908388
NA	12.364946	6.96849141	-1.77440787
MYHAS	13.270634	7.481936295	-1.773689848
PEX12	67.840146	38.28499267	-1.771977504
CPSF4L	16.832085	9.501383683	-1.771540357
ADH1C	17.75652	10.02593654	-1.771058519
ABHD12B	6.543118	3.698687443	-1.769037828
TUBA3D	7.4007802	4.18545958	-1.768212076
RNF144A	190.43918	107.7554575	-1.767327508
LOC101927734	6.2900968	3.560232702	-1.766765643
LOC101928387	8.6766623	4.911939596	-1.766443208
LINC00998	36.516673	20.67647834	-1.766097325
LENG9	36.130355	20.46082309	-1.765830971
LOC101928917	8.5080213	4.819023167	-1.765507445
TULP3	462.40976	261.9728854	-1.765105433
ROR2	7.966991	4.515647407	-1.764307594
LINC01208	6.4286302	3.645486324	-1.763449277
IGLV6-57	4.9087794	2.784582333	-1.762842271
ATP8B1	387.15306	219.7050842	-1.762148827
EFHC1	52.499981	29.80607581	-1.761385213
EFCAB5	7.3943981	4.200715973	-1.760270913
TTLL10-AS1	8.5534472	4.85962372	-1.760104837
OR52N2	7.1830612	4.081309965	-1.759989137

Supplementary table 4

Gene	Control	miR-1972	Fold change
IGFN1	8.4476536	4.98109265	-1.695943888
MCTS1	14.813145	8.7348968	-1.695857987
ZNF525	17.375198	10.2548594	-1.694337989
SNORD114-31	6.5876822	3.89007265	-1.693459943
MIR4421	7.1796704	4.24155625	-1.692697198
MIR548I1	6.6196186	3.91733769	-1.689825874
REP15	14.844854	8.79406152	-1.688054411
BAG2	61.856752	36.7168099	-1.684698426
DIO1	6.7677849	4.01768229	-1.68449977
LOC100996404	7.8801547	4.67947442	-1.683982852
LPHN3-AS1	7.1244157	4.23285413	-1.68312338
OR52E6	7.0815048	4.20875364	-1.682565773
CROCCP3	9.4084979	5.59356612	-1.68202139
LINC00998	36.516673	21.7106665	-1.681969233
FHL1	10.532043	6.26242238	-1.681784127
LOC284454	184.54259	109.780915	-1.68100793
NA	9.9308643	5.90807358	-1.68089719
SNHG20	42.503124	25.2963556	-1.680207389
ZFP3	52.773315	31.4261037	-1.679282784
COL4A6	9.1911727	5.47389933	-1.679090566
KRT42P	9.8574159	5.87183969	-1.678761081
AMT	16.000817	9.5333688	-1.678401165
FAM155A-IT1	14.209848	8.47145656	-1.677379602
DKFZp779M0652	20.45614	12.1976208	-1.677059856
KLF15	5.9794557	3.56552448	-1.677019958
LOC101927507	16.627679	9.91704733	-1.676676411
LOC101928464	27.203323	16.2250523	-1.676624671
DPY19L2	5.0528574	3.01531338	-1.675732084

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
POTEH	7.6814684	4.477266045	-1.715660475
LOC100653005	8.2475975	4.807507701	-1.715566158
PLAC8	127.6167	74.42260827	-1.714757185
LOC101929432	13.784772	8.048481311	-1.712717138
MCTS1	14.813145	8.649291965	-1.712642441
SCG3	6.7917452	3.968567132	-1.711384744
LOC101929679	7.4733866	4.367671161	-1.711068973
THAP10	55.660558	32.53037184	-1.711033547
PRDM5	26.556197	15.52990659	-1.710003636
SNORD111	72.030327	42.15860081	-1.708555909
SNORD101	20.04459	11.73598579	-1.707959606
NA	6.1594589	3.607288636	-1.707503765
A4GALT	22.52112	13.19596229	-1.706667487
IGFBP6	12.201261	7.150635989	-1.706318249
LINC01194	12.772876	7.487501393	-1.705893012
GGTA1P	5.691148	3.337367229	-1.705280726
FAM46A	16.559799	9.713659145	-1.704795111
MED4-AS1	10.944799	6.428630225	-1.702508718
NKAIN1	21.055153	12.38007987	-1.70072837
CIDECP	53.371316	31.38366217	-1.700608303
LOC101927497	37.474272	22.06217195	-1.698575813
LOC101928658	5.5818446	3.288982193	-1.697134326
LINC00472	59.726735	35.19296312	-1.69712153
LOC101059976	8.9313489	5.263639095	-1.696801164
ZFP2	10.930867	6.445113847	-1.695992822
MAPK8IP1	8.6663537	5.11582179	-1.694029624
ZNF816	22.672142	13.38418136	-1.693950606
ZNF561-AS1	17.479123	10.32003809	-1.693707183

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
PTP4A2	348.97662	198.4460988	-1.758546145
MIR3621	20.276513	11.53947187	-1.757143919
CD82	123.05928	70.03433475	-1.75712781
LOC100134368	12.110026	6.892304575	-1.757035772
IGLV3-9	23.84603	13.57250128	-1.756937002
ELOVL6	167.2797	95.23387113	-1.756514795
KCNIP2-AS1	8.5528727	4.875149353	-1.754381684
SYP	7.4736669	4.26179335	-1.753643652
SPATA31D3	10.421931	5.947410978	-1.752347487
SNORD115-2	5.6093418	3.202574953	-1.751509934
LEPREL1	25.230808	14.40523496	-1.751502701
NA	9.4270466	5.392323859	-1.748234494
NOX5	9.0679554	5.19115428	-1.746809078
GUCY1A3	21.236166	12.15753352	-1.746749565
SERPINA10	8.7054741	4.986291991	-1.745881328
HMHB1	6.9345143	3.973586643	-1.745152402
AADACP1	22.855167	13.10345467	-1.744209263
CHGB	8.1681129	4.682999802	-1.744205259
NA	23.000105	13.18913631	-1.743867407
CCND1	1328.9519	762.3157299	-1.743309017
GPR126	459.78029	263.9128545	-1.742167099
IL12A	13.322684	7.652155146	-1.741036901
DACH1	108.60191	62.38868489	-1.740730879
SNORD113-7	7.6202703	4.37802606	-1.740572164
NT5C3A	27.88769	16.02991109	-1.739728314
HDAC10	62.26814	35.81193924	-1.738753658
IRF2	431.11491	248.0241965	-1.738196963
LOC100130700	15.817066	9.099962305	-1.738146326

Supplementary table 4

Gene	Control	miR-1972	Fold change
NA	8.5552278	5.1054848	-1.675693514
APOL1	47.203826	28.1700235	-1.675675768
MIR1323	6.2131111	3.70799479	-1.675598671
SIRT4	9.9367275	5.93034471	-1.675573337
ATF3	119.71539	71.4577169	-1.675331806
LINC00862	5.5562696	3.31792436	-1.674622133
LINC00463	12.776857	7.63886333	-1.67261237
LOC101927144	11.880177	7.10308544	-1.672537598
PGBD2	21.552058	12.8892139	-1.672100295
PWAR4	6.3381577	3.79073022	-1.672014969
LOC101928162	13.777018	8.23991423	-1.671985581
MIR28	10.111839	6.04983642	-1.671423508
OR1S2	8.8921839	5.32616631	-1.66952803
LOC90246	19.510682	11.6867506	-1.669470188
PRIMPOL	69.223126	41.4941807	-1.668261071
LINC01350	4.8780558	2.92874171	-1.665580746
TRAJ5	8.7613765	5.26187993	-1.665065832
PAQR5	27.273715	16.3906847	-1.663976541
KCTD6	11.58359	6.96576128	-1.662932423
ADORA1	20.282599	12.1991491	-1.66262408
CDKN2A	10.811222	6.50584048	-1.661771759
FBLN7	12.23395	7.36518337	-1.66105163
TUBA3C	13.07791	7.87560913	-1.660558479
COX6A2	20.813442	12.5392541	-1.659862859
MTMR7	9.6935322	5.84243593	-1.659159345
SHISA9	8.1109742	4.89033904	-1.658570946
LOC101929058	9.0359666	5.44815936	-1.658535661
OR8H3	5.9725127	3.60121053	-1.658473626

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
GBP1	306.90235	181.262853	-1.69313427
DPY19L2P3	6.9522645	4.106184153	-1.693120495
LINC00276	6.0537091	3.578136804	-1.691860718
LENG9	36.130355	21.36438165	-1.691149115
MT4	18.284515	10.81811048	-1.69017639
LINC00052	5.7708688	3.414799752	-1.689958196
TAC1	8.3454718	4.939215142	-1.689635209
IL23A	13.682207	8.100337261	-1.689091058
LINC01343	6.1677696	3.651879907	-1.688930007
SIGLEC5	8.7456201	5.178627143	-1.688791228
LOC101927888	13.782619	8.171713615	-1.686625287
RRNAD1	25.357458	15.03953068	-1.686053826
HCRTR1	15.346346	9.103438173	-1.685774731
MIR1236	9.1810725	5.44691818	-1.685553598
SPIN2B	122.95207	73.01200639	-1.683997936
ZP3	15.782153	9.373327249	-1.683730119
INA	57.051799	33.90452558	-1.682719283
LOC101926966	15.67297	9.31732949	-1.68213109
MIR943	63.962851	38.03106314	-1.681858071
LINC00314	7.2696764	4.323108499	-1.681585452
IFIT5	83.269499	49.54411852	-1.680714109
FOXE3	7.0113906	4.174720729	-1.679487333
SNORD114-4	17.276567	10.2962692	-1.677944342
MIR1273F	6.2925792	3.752439748	-1.676930102
KCNG3	11.172878	6.665422889	-1.676244444
USP17L10	18.66616	11.13907512	-1.675736953
CPXM2	125.91009	75.16779947	-1.675053553
SNORD41	634.13301	378.6760416	-1.674605577

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
LOC101927206	8.6047277	4.953003931	-1.737274549
GAB1	222.20647	128.0611098	-1.735159648
ACE	153.04931	88.21936142	-1.734872146
LRRC16A	107.6031	62.03593708	-1.734528427
C6orf226	19.478199	11.23227346	-1.7341279
NDE1	382.21382	220.5314856	-1.733148536
MIR4472-1	5.8546242	3.379812593	-1.732233382
C1orf140	9.0456887	5.228296493	-1.730140724
NUDT17	29.294248	16.93336914	-1.729971635
FAM92A1P2	6.4670072	3.738318714	-1.729923974
NCF1C	10.351222	5.984512963	-1.729668192
SNORA37	70.881215	40.98696451	-1.729359955
ZNF322	35.645737	20.6159386	-1.729037812
LOC100505592	21.423305	12.39105603	-1.728932966
SNORD114-4	17.276567	9.992702103	-1.728918411
LOC101927888	13.782619	7.974675291	-1.728298435
IL17B	13.958291	8.076388546	-1.728283773
MIR3116-2	12.181144	7.049565527	-1.727928359
AMPH	158.19841	91.59063913	-1.727233412
OR2F2	5.4858077	3.177986958	-1.726189506
PIDD1	44.947914	26.04516454	-1.72576808
USP17L10	18.66616	10.8172811	-1.725587015
LOC101927757	5.76813	3.342962237	-1.72545472
MIR4502	10.868588	6.303596522	-1.724188475
RBBP9	148.43352	86.09323853	-1.724101975
RFTN2	40.588712	23.54660516	-1.723760669
COLEC12	207.10106	120.2466225	-1.722302487
TAL2	6.8425905	3.975700628	-1.721103051

Supplementary table 4

Gene	Control	miR-1972	Fold change
CISD3	86.507251	52.1630779	-1.658400047
ISG15	86.138685	51.9846078	-1.65700365
CHRNG	9.9579896	6.01103542	-1.656618019
MIR325HG	14.560617	8.79088024	-1.656332088
SEPP1	25.116469	15.1641566	-1.656305074
RDH14	45.46136	27.4551843	-1.65583882
KRTAP4-6	7.3737866	4.45416647	-1.655480691
PVRIG	11.646677	7.04242223	-1.653788459
LOC100653005	8.2475975	4.99065439	-1.65260843
ZBTB16	6.9431067	4.20130554	-1.652606941
SNORD114-14	39.890121	24.138504	-1.65255148
LOC101927721	6.78397	4.1059461	-1.652230659
ZNF300P1	14.804128	8.96523925	-1.651280846
LOC101929719	6.8849874	4.17070375	-1.650797511
MIR4312	16.608596	10.0659235	-1.649982358
TLCD2	12.65901	7.67602807	-1.64916155
RAB3IL1	79.178687	48.0216097	-1.64881368
CCNC	99.178654	60.1827599	-1.647957896
OLFML2A	9.0526005	5.49531043	-1.647331965
TUBA4A	21.496473	13.0514334	-1.647058421
PACSIN1	10.04335	6.10281599	-1.64569113
NUDT22	22.897655	13.9226073	-1.644638438
OR2L8	8.7438276	5.31675488	-1.644579794
FAM87B	8.4011562	5.11154709	-1.643564273
AKNA	24.907097	15.1592476	-1.643029867
OR6B3	4.7989855	2.92103841	-1.642903947
CCNA1	28.222686	17.1838473	-1.642396253
IGFBP3	54.011941	32.8884164	-1.642278542

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
BMP8B	11.195419	6.687592857	-1.674058175
LOC101926895	10.957284	6.545366159	-1.674052152
ATP6V0CP3	38.038193	22.72347987	-1.673959865
LINC01187	9.9033835	5.916698996	-1.673802155
C19orf44	41.826858	24.99474811	-1.673425879
PTCHD1	7.7425401	4.627591924	-1.673125079
ASPHD1	23.698675	14.16524188	-1.673015934
USP29	5.6542535	3.380310345	-1.672702472
ADH1C	17.75652	10.61799857	-1.672303892
ZNF503-AS2	8.8183893	5.276899392	-1.671130836
SNAR-I	312.07131	186.8020577	-1.670598866
NA	14.997819	8.977527356	-1.670595738
SAMD9L	188.65681	112.9500144	-1.670268128
NRG4	12.089954	7.242010002	-1.669419688
FAM129A	120.07271	71.93369555	-1.669213699
NEU3	18.457097	11.06389776	-1.668227354
PLCD4	17.508022	10.50044474	-1.66736008
SLC30A3	29.874641	17.91839837	-1.66726068
LOC101927372	5.658053	3.397666416	-1.665276201
ABCC6P2	7.5948634	4.561764429	-1.664896015
MAFG-AS1	27.287296	16.39537964	-1.664328402
IGFBP3	54.011941	32.49363936	-1.66223118
SNORD114-24	5.2956282	3.186485461	-1.661902529
PRPS1L1	9.2351294	5.560872557	-1.660733875
UBE2M	100.37973	60.45986773	-1.660270351
ZFAT-AS1	7.8062756	4.701980034	-1.660210286
LINC01176	8.3843313	5.051307951	-1.659833721
MIR3191	19.708338	11.90070463	-1.656064811

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
ZMYND8	491.04813	285.4120911	-1.720488179
ADAMTS12	6.9035997	4.017682286	-1.718304037
IPO13	111.15944	64.69682236	-1.718159144
LOC101929741	5.0268593	2.926981627	-1.717420864
ATP5SL	296.24579	172.5245354	-1.717122683
SUMO1	8.2937031	4.830409692	-1.716977155
FAM127A	16.727008	9.74424816	-1.716603273
CORO1A	108.20789	63.08691823	-1.715219205
CHRNG	9.9579896	5.808627028	-1.714344808
GDF7	10.944486	6.387788484	-1.713345101
ABHD14B	35.648352	20.82706681	-1.711635764
MRPL48	61.48909	35.92558697	-1.711568137
OR13C3	5.6206642	3.286434193	-1.710262202
KATNAL1	101.03009	59.08622552	-1.709875541
MIR891A	30.873533	18.05897138	-1.709595321
CENPM	43.566046	25.50618005	-1.708058437
HTN1	6.7728604	3.967078725	-1.707266445
PDPK1	429.68333	251.6893561	-1.707197063
ITGA11	25.126184	14.72695165	-1.706136132
CYP1B1	15.955155	9.353472018	-1.705800285
HAPLN3	200.1042	117.3787396	-1.704773839
NUDT4	94.038512	55.17083655	-1.70449676
LRRC71	12.965498	7.614009675	-1.70284765
CYP2B7P	6.5890993	3.870325525	-1.702466441
LOC100506100	38.353733	22.53149888	-1.70222734
PBXIP1	88.967516	52.26662855	-1.702185862
PAPSS2	386.16525	227.0253608	-1.700978468
LOC100130899	8.1781793	4.809766393	-1.700327752

Supplementary table 4

Gene	Control	miR-1972	Fold change
OR52N2	7.1830612	4.37858607	-1.640497888
IL34	13.722475	8.36883424	-1.63971167
PLEKHM1	134.99351	82.4093737	-1.638084456
SCARNA20	32.691326	19.9762773	-1.636507398
SNORA36B	6.631221	4.0523929	-1.636371688
CD101	7.3373882	4.4867038	-1.635362737
IL6	236.85212	144.873494	-1.634889271
SH3GL3	6.6196735	4.05200994	-1.633676512
ZBTB12	18.592708	11.3818306	-1.633542834
FAM90A25P	18.293829	11.2051588	-1.632625614
LINC01476	6.4914345	3.97823824	-1.631735996
OXCT2	7.637276	4.68166933	-1.631314695
ZBTB44	218.74486	134.115828	-1.631014519
MIR520F	9.5227824	5.84001915	-1.630608084
DKFZP434L187	5.5436777	3.40188785	-1.629588614
EGLN3	8.4714566	5.20177644	-1.628569906
ALG10B	11.202913	6.87933714	-1.628487255
MIR3130-1	11.434813	7.02174474	-1.628485947
PCDHB14	14.096632	8.65707824	-1.628335947
IGKV3-20	15.354057	9.43025099	-1.628170531
LOC101927746	29.936544	18.3969138	-1.627259001
MIR598	7.1384512	4.3887279	-1.626542209
PTTG1	50.47561	31.0393279	-1.62618244
KRTAP19-3	5.6738898	3.49055378	-1.625498474
LOC101928004	18.023695	11.088755	-1.625402904
TNFAIP3	550.12826	338.636221	-1.624540506
LOC100289361	13.425916	8.26966698	-1.6235135
PNMAL2	10.589205	6.52268873	-1.62344179

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
DAPL1	5.3887783	3.25432877	-1.655880126
C17orf96	20.494088	12.37962121	-1.655469695
NPTX2	33.266315	20.09646316	-1.655331845
LOC101927720	10.514058	6.352611224	-1.655076537
R3HDML	6.1861178	3.738381074	-1.654758483
ZNRF2P1	14.446192	8.737451694	-1.653364423
TNF	19.45505	11.78020489	-1.651503496
LINC01490	11.376261	6.889386482	-1.651273524
URAHP	24.201609	14.66667739	-1.650108526
LINC00278	10.329464	6.264547227	-1.648876432
TUBB2A	44.062647	26.73490388	-1.648131854
LINC01347	14.576222	8.84449647	-1.64805564
FAM73B	46.596754	28.27792674	-1.647813672
MIR4638	40.996316	24.88665032	-1.647321593
C10orf53	6.6465188	4.035547333	-1.646993147
JDP2	18.15658	11.02612658	-1.64668708
SNORA44	69.617713	42.28367524	-1.646444217
LOC101928227	5.8825058	3.575609743	-1.645175575
SURF2	98.954833	60.1713157	-1.64455159
RRP8	67.895801	41.29818951	-1.644038202
ZNF705A	4.5406972	2.763536766	-1.643074639
LOC101929463	9.9281657	6.042739886	-1.64299075
CEBPA	12.663081	7.711476635	-1.642108425
PAQR5	27.273715	16.61394412	-1.641615897
VPS37C	121.95383	74.30625342	-1.641232331
ARL11	8.7718139	5.346490377	-1.640667665
CHRNG	9.9579896	6.071941443	-1.640000925
MVK	28.024697	17.09370742	-1.639474456

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
MAGEA12	5.8002235	3.412411847	-1.699743114
LOC100130673	6.2766898	3.693878466	-1.699213947
CXorf31	10.865206	6.398642098	-1.698048793
TRAV13-2	14.772022	8.700603752	-1.697815743
MCU	266.59468	157.0353804	-1.697672734
PCDHGA10	67.715964	39.89805269	-1.697224781
IRF6	139.27808	82.06660722	-1.697134674
ARHGAP28	178.90416	105.4217831	-1.697032241
ANKRD65	13.569421	8.000339501	-1.696105675
OR4D1	6.2658496	3.69431475	-1.696078991
GPR135	24.556708	14.47886282	-1.696038459
TIMP3	106.20902	62.63836673	-1.695590542
OR7E14P	8.0804765	4.771126654	-1.693620213
TTC9	16.415927	9.695527872	-1.693144249
LOC101060400	8.6568048	5.115760431	-1.692183386
SDC3	374.67076	221.4621718	-1.69180479
KRTAP12-1	10.344794	6.115558908	-1.691553377
LOC101928221	5.9291585	3.505554995	-1.691360857
OR10A3	23.34467	13.80766273	-1.690703923
ATL1	21.844982	12.93184058	-1.689239946
SNN	303.29142	179.7431842	-1.687359786
SEMA6C	24.978045	14.80925994	-1.686650477
CCNT1	254.70048	151.0826569	-1.685835349
LOC101927002	28.64437	16.99150883	-1.685804975
SYN2	24.969333	14.81491413	-1.685418649
TRBV4-1	7.8426232	4.654129013	-1.685089337
ZNF552	8.462102	5.022435717	-1.684860188
NA	7.726902	4.587060262	-1.68449977

Supplementary table 4

Gene	Control	miR-1972	Fold change
ZNF708	14.987492	9.23400918	-1.623075313
AHSG	9.8967948	6.0981364	-1.622921193
NR4A1	34.973506	21.5508749	-1.622834603
CYP2D7P	16.948262	10.4436531	-1.622828906
CXCR5	7.7152904	4.7544018	-1.622767852
MYL1	11.361871	7.00317532	-1.622388505
GATA6-AS1	10.662148	6.57215745	-1.6223209
RNU6-68P	4.9573089	3.05630369	-1.621994878
C1QTNF9B-AS1	16.089715	9.92276832	-1.621494614
FAM138C	3.6419245	2.24663254	-1.621059278
TRMT61A	62.671316	38.704219	-1.619237317
LOC101928947	5.459051	3.37363739	-1.618149883
LOC643406	4.9301403	3.0468828	-1.618093198
PRKY	20.001295	12.3688811	-1.617065825
NPY1R	9.5786254	5.92371006	-1.616997683
LOC645513	21.94902	13.5780574	-1.616506622
GRM3	6.4278273	3.97715149	-1.616188705
SFRP5	11.87166	7.34552508	-1.616175843
OR10H4	8.5093634	5.2669779	-1.61560644
MIR4492	32.158181	19.9061163	-1.615492492
ZNF823	57.600836	35.6660412	-1.615005041
AMELX	5.6646627	3.50843553	-1.614583664
ZNF594	24.824052	15.3779833	-1.614259238
AOC3	10.797622	6.69474295	-1.61285088
HHAT	19.280302	11.9682229	-1.610957794
CDY2B	12.785609	7.93697798	-1.610891321
FOXL2NB	9.274111	5.75729798	-1.610844356
LIG3	83.822854	52.0611713	-1.610083912

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
LOC283278	6.7006213	4.093947219	-1.636714149
RNF217-AS1	7.8931247	4.825564284	-1.635689475
ISL1	16.029168	9.802757332	-1.635169301
TRIM3	60.696614	37.12948314	-1.634728213
C8orf31	12.22449	7.479196522	-1.634465731
LOC391722	10.79298	6.60394203	-1.634323908
LOC100287010	5.7428701	3.51535959	-1.633650817
CD70	13.9535	8.544071462	-1.633120658
ELAVL3	19.486017	11.94198572	-1.631723379
LINC00475	4.7578362	2.916423518	-1.631394145
LLPH	132.61713	81.31410992	-1.630923899
TNFSF18	331.17676	203.1123757	-1.630510015
PRR13	48.626621	29.82782142	-1.6302438
EXOSC4	38.975085	23.90826258	-1.630193101
LOC101928758	14.345728	8.801800687	-1.629862867
PWP2	170.46748	104.597962	-1.629739975
PGBD2	21.552058	13.22593267	-1.629530326
SNORD63	324.90191	199.3939649	-1.629447072
DHX58	18.842387	11.56406745	-1.629390987
C9orf116	72.395943	44.43677943	-1.629189687
LOC101927757	5.76813	3.540695203	-1.629095316
RPS15AP10	11.545018	7.087808848	-1.628855656
ZNF33B	98.773824	60.67335101	-1.627960582
ZNF300P1	14.804128	9.094090608	-1.627884358
AMZ2P1	6.2614768	3.846412677	-1.627874418
DNM1P35	15.4841	9.513672923	-1.627562765
CELP	8.7666139	5.387059067	-1.627346906
ZNF132	16.919226	10.39712753	-1.627298144

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
GDPD5	57.180781	33.98631668	-1.682464786
LOC101929715	11.456978	6.810265173	-1.682310132
GIPC2	74.711408	44.41548255	-1.682102811
LOC101927685	13.020529	7.742142025	-1.68177348
NT5M	10.810853	6.428667114	-1.681663155
PPP3CB-AS1	27.810221	16.53861262	-1.681532898
RBP1	51.001862	30.33273842	-1.681413058
RPL13A	40.346315	24.00038845	-1.681069247
EPS15L1	405.55254	241.2708687	-1.680901382
MAP2K6	88.806997	52.86197195	-1.679978893
DZIP1L	25.758688	15.33419319	-1.679820234
CREB3L2	610.38078	363.3957256	-1.67965867
PABPC3	7.0355708	4.189397498	-1.679375335
MIR27A	32.473905	19.34560562	-1.678619207
LINC00906	5.9607095	3.551005614	-1.678597589
LOC100505478	7.1269451	4.245851381	-1.678566773
AKT2	133.26008	79.39962128	-1.678346505
SEMA6A	22.09301	13.16770165	-1.67781822
SNORD90	13.086034	7.802532796	-1.677152103
SPATA3-AS1	8.4756234	5.054445545	-1.676865112
GDF6	119.55904	71.30852122	-1.676644475
MIR550A1	7.891342	4.708098751	-1.676120756
LOC284600	8.9790825	5.357119918	-1.676102576
MIF4GD	72.232508	43.13487517	-1.674573256
SIRPA	489.1068	292.1291506	-1.674282771
LGI3	7.4462784	4.447837299	-1.674134624
CRHBP	10.600431	6.333432052	-1.673726114
LOC101927257	8.9728071	5.361537112	-1.673551241

Supplementary table 4

Gene	Control	miR-1972	Fold change
POM121L8P	69.141378	42.9656255	-1.609225458
LOC284344	8.4920666	5.27748698	-1.609111808
LOC101927151	13.318803	8.28283848	-1.607999819
CELF4	10.005029	6.22366627	-1.607577989
SNORD58C	124.75338	77.6213165	-1.607205103
SPATA24	18.067345	11.2484197	-1.606211834
CXorf31	10.865206	6.76537112	-1.606003026
CBX4	114.48654	71.289646	-1.605935056
MYRF	10.370186	6.46179686	-1.604845569
HMSD	8.04396	5.01263022	-1.604738362
GP9	10.49286	6.53875806	-1.604717612
KCNK3	20.878303	13.0132652	-1.604386221
ZNF573	14.286299	8.90558155	-1.604196134
IGHV1-24	7.4617661	4.6537379	-1.603391998
ZNF468	258.28737	161.112841	-1.603145798
TEX15	12.392753	7.73428946	-1.602313052
CASP12	16.803484	10.4882625	-1.602122781
ZNF204P	8.0758177	5.04177001	-1.601782245
KRTAP5-8	9.025871	5.634931	-1.601771347
MIR103A2	15.848983	9.89512105	-1.601696699
TUBGCP6	38.633378	24.1449046	-1.600063396
ZNF276	59.76321	37.3605938	-1.599632238
LOC101926940	9.4448958	5.90784029	-1.598705331
MIR27A	32.473905	20.3128711	-1.598686126
MTOR-AS1	6.508771	4.07268094	-1.598153925
LOC101060400	8.6568048	5.41700291	-1.598080149
MIR4311	5.8984819	3.69217982	-1.597560839
DIAPH3-AS1	11.643144	7.29278105	-1.596530054

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
STAT5A	135.20514	83.11205072	-1.626781454
FAM76A	29.249375	17.98634304	-1.626199123
PCDHGA8	11.531116	7.090993488	-1.626163641
INPP5E	57.305745	35.26422957	-1.625038892
LOC101928162	13.777018	8.478345791	-1.624965309
C9orf106	27.446344	16.89525005	-1.624500585
ZKSCAN5	43.034018	26.49311288	-1.624347348
OR1L3	3.9433558	2.430677621	-1.622327762
LOC100653133	21.809327	13.44388707	-1.6222486
C17orf97	40.282383	24.84950196	-1.621053952
SH3RF2	40.846284	25.19798544	-1.621013885
HAAO	14.174662	8.744641171	-1.620954152
SCARNA21	100.32514	61.92972823	-1.619983478
EBF4	17.281177	10.66775208	-1.619945493
NA	8.9715733	5.539233207	-1.619641741
LINC00536	8.0239181	4.954864159	-1.619402237
MMP17	41.805452	25.81632546	-1.619341674
ZNF679	5.2305413	3.230168828	-1.619278008
MIR1185-2	8.6446336	5.338592085	-1.619272169
SNORD115-24	8.0006711	4.942028575	-1.61890426
HIST1H4H	39.300629	24.28116259	-1.618564549
HDHD2	136.94102	84.6487466	-1.617756068
RIIAD1	9.2316613	5.706857685	-1.617643519
LOC101927204	39.647449	24.51225302	-1.617454286
CXCL8	3013.9613	1863.646364	-1.617238825
SNORD19	7.838496	4.852703008	-1.615284503
LOC101929445	9.3749672	5.804315223	-1.615171957
GRIN3B	14.259731	8.828882411	-1.615122958

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
G6PC3	836.29765	500.139057	-1.672130266
LRRN4	6.9525587	4.160021376	-1.671279549
MS4A6A	8.0245038	4.802305654	-1.670968991
DOCK1	397.86394	238.1125276	-1.670907227
LOC101929340	19.210922	11.50068995	-1.670414773
C14orf178	9.4277121	5.647882538	-1.669247206
CAMK4	62.153491	37.25517593	-1.668318272
IL1F10	6.4887565	3.891538937	-1.667401161
ZNF599	10.493422	6.299458061	-1.665765898
LINC00263	39.673154	23.82170848	-1.665420179
NFKBID	44.558207	26.76212774	-1.664972522
LOC100996286	10.563336	6.344588144	-1.664936507
OR4A47	6.0046764	3.60681265	-1.664815155
C1R	26.947574	16.18931173	-1.66452871
MILR1	14.534222	8.732630808	-1.664357723
PCGF3	378.56421	227.548354	-1.663664909
LRRC37B	28.8035	17.31341069	-1.663652535
PITX2	8.3642325	5.028877424	-1.663240487
LOC392196	8.4948031	5.109375933	-1.662591133
KRTAP5-6	9.332258	5.616133312	-1.661687401
TRIM49	6.3862892	3.843292006	-1.661671594
PBX1	80.863841	48.6679948	-1.661540431
CLIP2	133.58483	80.41625676	-1.661167014
DCAF12L2	7.9383919	4.779206724	-1.661027097
BCL2	30.344731	18.26975021	-1.660927504
C10orf55	11.348034	6.832353743	-1.660925965
NBPF1	165.81751	99.87284495	-1.660286189
VWA5A	60.030983	36.16553222	-1.659894924

Supplementary table 4

Gene	Control	miR-1972	Fold change
CEBPA	12.663081	7.93199501	-1.596455966
BAK1	155.04775	97.2117427	-1.594948805
IL17B	13.958291	8.75240152	-1.594795582
PLBD1	11.904838	7.46543716	-1.594660485
CCL18	19.072468	11.9653257	-1.593978186
CHKB-AS1	25.884725	16.249799	-1.592925828
CMA1	10.484304	6.58450484	-1.592269103
PRIM2B	130.33039	81.9240939	-1.590867588
OR8B4	5.3961111	3.39355445	-1.59010595
MIR4472-1	5.8546242	3.6829745	-1.589645596
ATP5L	37.741676	23.7467242	-1.589342436
CDH20	6.9380169	4.36572604	-1.589201158
GBP5	10.43691	6.57019772	-1.588523008
IFT81	51.292512	32.3163412	-1.587200487
IGKV1-8	5.6086441	3.53471868	-1.58672999
MAL2	200.09982	126.112094	-1.586682232
LOC339622	5.1025726	3.21723419	-1.586012172
NPL	18.449712	11.6345918	-1.585763607
KRT38	13.153941	8.29566167	-1.585640946
PRSS21	9.4484871	5.96096209	-1.585060756
LINC00276	6.0537091	3.81983187	-1.584810356
SLC30A10	6.3791496	4.02737731	-1.583946358
OR52M1	7.363391	4.64925568	-1.583778463
ALOX5AP	23.134325	14.6083281	-1.583639475
MIR147A	16.589357	10.4787994	-1.583135236
CXCL2	48.698467	30.7627942	-1.583031317
HNF4A	14.313027	9.04537056	-1.582359394
C3orf67	20.371689	12.8755145	-1.582203841

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
ANKRD53	34.739232	21.50970829	-1.615048962
NOG	40.346315	24.99648234	-1.614079709
EGR3	14.718184	9.119490881	-1.613926093
LARS2-AS1	6.89447	4.273850589	-1.613175243
LOC100506538	6.7682885	4.195753393	-1.613128289
GKAP1	10.315636	6.395414083	-1.612973944
LOC101928399	13.422012	8.323276713	-1.612587511
CACTIN	70.679695	43.84391872	-1.612075213
PRKCZ	13.177904	8.175832918	-1.611811856
PBOV1	7.026481	4.363113262	-1.61042828
ZBTB12	18.592708	11.54585291	-1.610336454
LINC01470	5.927864	3.681962064	-1.609974223
LOC101060264	30.681669	19.06100976	-1.609656014
MIR3074	5.2605729	3.270066601	-1.608705118
LINC01476	6.4914345	4.037261695	-1.607880547
ATP6V1E2	16.398019	10.19978005	-1.607683549
CYB561D1	30.52403	18.99030198	-1.607348308
ZNF135	43.033387	26.80058828	-1.605688151
AHI1	62.174339	38.72593639	-1.605496069
GPNMB	12.868266	8.015937205	-1.605335133
TMEM110	50.200965	31.29824464	-1.603954636
LOC100506476	7.9773034	4.974855495	-1.603524646
ZNF707	27.110236	16.91372647	-1.602854092
IRF7	31.911893	19.91035864	-1.602778411
SPATA25	18.462481	11.52091201	-1.602519027
LOC100506371	9.5468404	5.963659893	-1.600835819
LOC101928762	8.8180294	5.512312279	-1.599696999
LOC101927903	10.698698	6.689333405	-1.599366761

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
SEPT7	778.56766	469.2013046	-1.659346742
MN1	77.744121	46.85398887	-1.659285012
JMJD8	238.79984	143.9297375	-1.659141743
LOC90246	19.510682	11.76355353	-1.658570406
FAM205A	8.6669624	5.226717202	-1.658203814
RPS3A	17.800736	10.73556762	-1.65810852
OR10V2P	6.7128918	4.0503785	-1.657349257
NRN1	206.18782	124.4473018	-1.656828366
FSTL5	13.349232	8.059053153	-1.656426802
NA	5.6735258	3.42546119	-1.656280855
SDPR	1178.2228	711.9317447	-1.654966026
ZNF772	35.834105	21.65768498	-1.65456766
LILRA5	5.8217704	3.518794007	-1.65447888
SLC9A1	445.32466	269.2024856	-1.654236793
MZF1-AS1	15.172461	9.173112337	-1.654014509
DPPA4	6.7677849	4.09870643	-1.651200203
CD34	461.74238	279.6952564	-1.650876676
NHEJ1	178.85059	108.4004444	-1.649906466
TEX15	12.392753	7.516990045	-1.648632348
IL20RB	52.219605	31.67927718	-1.648383725
MIR544B	6.3950783	3.880955888	-1.647810091
LOC101926966	15.67297	9.513754328	-1.647401127
MYH6	7.5979304	4.612764454	-1.647153349
ITGB3BP	77.389881	46.99631646	-1.646722273
MYO5C	60.640766	36.82946387	-1.646528605
LOC101927144	11.880177	7.216249309	-1.646309178
CCDC97	371.42634	225.612126	-1.646304843
NOS1	24.134995	14.66652949	-1.645583241

Supplementary table 4

Gene	Control	miR-1972	Fold change
GGT8P	6.8718348	4.34440026	-1.581768343
PCDHA6	10.661301	6.74251094	-1.581206364
ANKRD29	12.662291	8.01331136	-1.580157151
MIR219A2	12.300864	7.78521293	-1.580029261
IRS1	13.456463	8.51753027	-1.57985502
HES3	8.79323	5.56755567	-1.579369937
CSF2	24.659026	15.6151158	-1.579176645
LOC101927354	9.2274092	5.84426503	-1.578882735
ZNF583	58.564464	37.1094969	-1.578153015
ELN	10.205472	6.47882359	-1.575204441
PRKCZ	13.177904	8.36801908	-1.574793784
SAPCD2	30.406387	19.3104792	-1.574605534
PSKH2	10.959474	6.96016455	-1.574599776
LOC100505478	7.1269451	4.52662886	-1.574448727
LOC285043	7.2415987	4.60078546	-1.573991818
TECTA	10.226161	6.49915552	-1.573460036
C3orf80	7.4027457	4.70553906	-1.573198222
ASIP	9.3894691	5.96899099	-1.57304126
DRD3	8.2932979	5.27309445	-1.572757319
DUOX2	6.653422	4.23154385	-1.57233914
ZFP69	28.145345	17.9154626	-1.571008529
CLN8	76.484487	48.6878588	-1.570914989
STAG3L4	36.71368	23.3758622	-1.570580785
PDE1C	7.5748396	4.82593804	-1.569609787
CXCL5	175.23017	111.651134	-1.569443715
C1QTNF3	6.7129733	4.27753545	-1.569355395
LOC283693	7.8214227	4.98626168	-1.568594509
BAAT	6.0852048	3.87965328	-1.568491909

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
S100A3	52.476568	32.815678	-1.599130991
TPI1P2	19.049673	11.9132142	-1.59903723
ANGPTL4	101.09385	63.2381245	-1.59862185
KIAA1804	15.405794	9.637268756	-1.598564305
PNMT	9.0330631	5.650746651	-1.598560984
MIR711	6.861034	4.296303749	-1.59696203
OTOR	5.4110058	3.38843389	-1.596904636
SIRT7	84.303815	52.79486567	-1.596818447
KLHDC8B	63.046316	39.49359928	-1.596367939
SNORA13	100.82098	63.19249198	-1.595458253
TLE6	9.1370933	5.727175877	-1.595392474
SNORA16B	20.142813	12.62748719	-1.595156046
ZNF136	60.827665	38.13375581	-1.595113413
MYOC	8.920889	5.598117478	-1.593551589
USP9Y	26.426528	16.59017522	-1.592902304
HS3ST1	32.231698	20.23989136	-1.592483737
LOC101927797	5.6095315	3.522590737	-1.592444842
LOC101928374	9.2296894	5.79910836	-1.591570429
ZNF296	69.77364	43.83984539	-1.591557628
RAB33A	11.399986	7.165182413	-1.591025281
WNT4	16.200032	10.18290356	-1.590904945
NA	8.5552278	5.380740871	-1.589972082
GNAS-AS1	6.7462124	4.24348102	-1.589782629
SNORD114-6	9.5226831	5.992389971	-1.5891294
LOC101929741	5.0268593	3.163325792	-1.589105784
TPI1P3	7.5627276	4.760941169	-1.588494243
ZNF324	23.956015	15.08340738	-1.58823631
KANSL1L	50.708204	31.95470584	-1.586877506

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
SNRPA1	50.360161	30.60886816	-1.645280065
ACVR2B	36.354934	22.11919914	-1.643591771
PRAP1	33.56208	20.42151111	-1.643467007
MGP	694.60513	422.6608802	-1.643410028
LOC101927497	37.474272	22.81349186	-1.642636379
KANK4	6.0866844	3.712853771	-1.639354741
SNORA7B	83.628612	51.02019449	-1.639127658
BEAN1	16.271324	9.92710827	-1.639079898
VILL	13.160789	8.030371119	-1.638876775
LOC100506302	28.034177	17.11736309	-1.637762613
PRICKLE2-AS3	8.5089313	5.195941908	-1.637610934
IGKV1-27	5.8940027	3.600308771	-1.637082547
EPN2-AS1	6.5168013	3.982919056	-1.636187234
OR5AR1	12.000451	7.334907376	-1.636073926
PBX2	322.56598	197.1993826	-1.635735232
NA	11.416779	6.980226639	-1.635588564
NA	10.814676	6.612196708	-1.635564701
REEP5	885.20649	541.3074196	-1.635311949
PIK3IP1	42.489729	25.98848798	-1.634944244
LOC101929229	21.159847	12.94283805	-1.634869182
ATP8B4	6.6273415	4.055585297	-1.63412701
PLCE1-AS2	18.655915	11.41747188	-1.633979525
ABCB6	49.243066	30.18302044	-1.631482363
LOC101926901	10.828049	6.637495537	-1.631345555
TRAJ53	4.8602841	2.979635072	-1.631167566
ATP5L	37.741676	23.14747471	-1.630487858
LOC100996404	7.8801547	4.833782622	-1.630225292
ZNF492	7.2204066	4.431944654	-1.629173462

Supplementary table 4

Gene	Control	miR-1972	Fold change
LAMP3	46.556801	29.701375	-1.567496501
UTS2	6.8898436	4.39589627	-1.567335349
SLC25A25	41.547509	26.5250489	-1.566349956
SDC4P	8.6874234	5.54700936	-1.566145437
CELP	8.7666139	5.59777372	-1.566089367
TMEM134	38.528261	24.60222	-1.566048151
PDF	95.571317	61.0359289	-1.565820639
SNHG7	57.041024	36.4351093	-1.565551053
RPS3A	17.800736	11.3785693	-1.564408995
FLJ38668	26.201538	16.7507506	-1.564200811
DUSP26	11.284021	7.21587485	-1.563777283
BOLA3-AS1	42.085855	26.9178173	-1.563494343
RILP	25.094748	16.0563805	-1.562914353
TKTL1	11.676815	7.47151589	-1.562844113
KRTAP5-6	9.332258	5.97182989	-1.562713297
LOC101927341	6.1504502	3.938251	-1.56172123
ZNF611	76.909912	49.2594089	-1.561324294
ST3GAL5-AS1	10.855012	6.9528676	-1.561228118
OARD1	150.42482	96.3909173	-1.560570475
INSRR	7.2677579	4.657263	-1.560521247
GATS	9.2196944	5.9081151	-1.560513677
FABP6	6.3608247	4.07798704	-1.559795215
ZNF136	60.827665	38.9975256	-1.559782689
SBDSP1	23.506547	15.0923649	-1.55751247
FAM131C	11.368438	7.30531352	-1.556187545
FAP	24.910904	16.020419	-1.554947067
ATP8B4	6.6273415	4.26256799	-1.554776719
INAFM1	52.163686	33.5585105	-1.554410042

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
GEMIN8	41.716992	26.29087235	-1.586748103
RUSC1-AS1	14.371101	9.058338881	-1.586505134
OR13J1	10.900323	6.871008793	-1.586422507
ZNF276	59.76321	37.67266343	-1.586381341
LOC101929637	6.4286302	4.052575506	-1.586307329
EFNA3	39.619017	24.97880182	-1.586105578
C15orf48	8.6895801	5.478847514	-1.586023352
PRG2	11.113395	7.013059458	-1.584671507
C19orf48	139.29632	87.91956788	-1.584360786
LOC146880	66.648582	42.07995799	-1.583855727
NLGN4Y-AS1	6.5857947	4.158278846	-1.583778994
PSG1	4.9519256	3.128056516	-1.583067814
MIR16-2	7.4351042	4.69665286	-1.583064445
LINC00326	5.3813967	3.400207983	-1.582666919
NA	5.9609049	3.766699452	-1.58252734
IQCF5	7.8129802	4.937687083	-1.582315775
LOC148696	8.8760578	5.611105855	-1.581873176
NA	5.6735258	3.587425751	-1.581503335
TRIB3	92.972289	58.81030906	-1.580884214
USP27X	39.179744	24.78450595	-1.580816012
AADACP1	22.855167	14.45786148	-1.580812421
CASC1	7.4049598	4.684873414	-1.58061044
HRG	5.3827922	3.406980525	-1.579930421
CLEC18A	7.9861523	5.055155275	-1.579803553
MRGPRX3	5.2835252	3.348164159	-1.578036494
OR13C3	5.6206642	3.561844424	-1.578020685
OR5T1	3.8610319	2.448460864	-1.576922047
LOC101927837	7.4135184	4.701954495	-1.576688677

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
FGD5P1	9.3435855	5.735479179	-1.629085415
MYD88	390.68347	239.8624879	-1.62878103
LTB4R	15.754141	9.673802515	-1.628536505
TLE6	9.1370933	5.610826264	-1.628475533
UCP2	34.182737	20.99838101	-1.62787489
SNHG7	57.041024	35.04274885	-1.627755403
AGPAT4-IT1	14.568217	8.952072016	-1.62735701
GH2	8.2715606	5.088182556	-1.62564147
LOC642934	5.8932063	3.628561841	-1.624116253
CYP4X1	11.995216	7.386935002	-1.623842045
SATB1	69.318551	42.69457279	-1.623591635
ZNF589	96.393422	59.3766029	-1.623424327
RGPD4-AS1	6.7100241	4.133701486	-1.623248352
C11orf40	10.528339	6.487659884	-1.622825343
RGCC	214.12649	131.949707	-1.622788683
RAB5B	200.68912	123.6811793	-1.622632689
SNORD114-13	7.7633674	4.785676961	-1.622208818
IGHV4-34	12.42459	7.659940937	-1.622021693
LOC644656	17.728187	10.93831567	-1.620741899
TLR1	59.800952	36.91404599	-1.620005341
LINC00595	8.195592	5.059017518	-1.619996754
PTGFR	12.765811	7.885116668	-1.618975518
C1RL-AS1	11.418282	7.053003895	-1.618924672
VPS36	144.56627	89.31118036	-1.618680522
HDAC8	54.971946	33.98747655	-1.617417701
LUC7L2	97.361092	60.19888234	-1.617323909
LAMC2	245.05584	151.5368275	-1.617137224
IGHV1-2	14.146971	8.748657619	-1.617044797

Supplementary table 4

Gene	Control	miR-1972	Fold change
GSTM2	12.356682	7.94952826	-1.554391806
THBS4	8.0694481	5.19249912	-1.554058628
LINC01341	6.2882809	4.04752121	-1.55361283
NRG4	12.089954	7.78442276	-1.553095773
SPINK1	6.9072396	4.45100504	-1.551838195
ZNF19	11.913117	7.6808591	-1.551013608
C11orf96	35.819422	23.0955336	-1.550924184
MIR891A	30.873533	19.9169018	-1.550117246
LOC101927156	5.1359573	3.31329777	-1.550104353
ZNF154	30.789135	19.8640576	-1.549992226
HTR1F	6.9598382	4.49145529	-1.549573074
TRIM6	22.12907	14.2838824	-1.549233558
LOC100996342	6.9769159	4.50348311	-1.549226609
LINC00690	7.6899102	4.96397653	-1.54914315
GPRIN2	12.00677	7.75406804	-1.548447806
NLGN4X	7.0342302	4.54516572	-1.547628993
FAM157A	6.5448995	4.22911142	-1.547582653
LOC100996286	10.563336	6.82577525	-1.547565812
ECEL1	9.3097982	6.01788881	-1.547020637
FAM107A	24.972586	16.1470048	-1.546576999
TAC4	10.229883	6.61596159	-1.546242769
ABTB1	14.090278	9.11666972	-1.545550977
ZNF844	46.541586	30.114768	-1.545473845
C15orf43	6.3887427	4.13391401	-1.545446447
MIR614	68.999794	44.6875962	-1.54404802
MIR30B	4.8483045	3.14083075	-1.543637634
AQP3	10.523336	6.82384133	-1.542142582
WI2-2373I1.2	15.197573	9.85624641	-1.541923045

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
ZNF624	55.186323	35.03224038	-1.575300992
OR2T35	10.087852	6.406246126	-1.574689967
MTMR8	16.885073	10.72896039	-1.573784633
LOC100288798	23.588847	14.9887461	-1.573770567
ICAM1	2867.665	1822.951447	-1.573089093
SNORD100	996.29554	633.539114	-1.572587254
KITLG	588.46447	374.3819566	-1.571829147
LOC344887	23.222836	14.77517035	-1.571747414
FLJ45743	6.4539028	4.106726734	-1.571544243
FLJ37505	7.4090032	4.716131565	-1.570991634
LOC642846	12.251441	7.800576903	-1.57058135
COL13A1	95.056383	60.53915904	-1.570163581
USP17L5	17.363098	11.06031167	-1.569856113
SUN5	9.1967811	5.858487309	-1.569821803
HRH1	30.919114	19.70173846	-1.56935968
HERC6	143.12542	91.20980384	-1.569188973
MIR3144	4.5927344	2.927721475	-1.568706066
LOC100506123	24.377362	15.54624211	-1.56805494
ARHGEF25	34.176077	21.80024118	-1.567692611
LINC00467	19.909468	12.70148345	-1.56749155
IGBP1P1	11.212708	7.15369216	-1.5674015
NHLRC1	23.402276	14.93091039	-1.567370997
THAP3	32.610594	20.80649475	-1.567327622
MIR134	15.089772	9.628034476	-1.567274383
FAM104A	50.811901	32.42760644	-1.56693345
LOC101929726	10.449781	6.671162975	-1.566410663
HLA-B	1082.5287	691.2707987	-1.565998064
KIAA0513	43.988029	28.10635992	-1.565056057

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
CDH12	10.579262	6.544071864	-1.616617628
OR7G3	5.3420884	3.306317508	-1.615721522
LOC101929058	9.0359666	5.593566117	-1.615421433
EPOR	74.187456	45.94047197	-1.614860563
NID1	685.77986	424.9604793	-1.613749738
LOC101929224	10.432801	6.465431193	-1.613628069
MGARP	126.60233	78.46365393	-1.613515542
LINC00707	8.2371416	5.106926067	-1.612935346
C17orf58	23.045195	14.29261718	-1.612384575
LOC101929462	6.1252967	3.801928104	-1.61110271
SLFN12L	5.1662313	3.209608942	-1.609613957
NA	23.946665	14.89143236	-1.608083355
DBIL5P	9.5130634	5.91598726	-1.608026344
RIPK3	15.659196	9.738650643	-1.60794308
DHCR24	411.231	255.7713461	-1.607807139
PTPN4	54.65228	34.02638144	-1.60617372
ZNF350-AS1	9.5619989	5.955372745	-1.605608808
SLC22A31	14.002733	8.72472494	-1.604948365
NA	14.760277	9.200103417	-1.604359946
ZCWPW2	4.9792988	3.103624203	-1.604349764
MIR4292	16.460554	10.2622321	-1.603993579
NBR2	17.654719	11.00957013	-1.603579336
HTR1F	6.9598382	4.340518859	-1.603457652
TRIM2	54.289684	33.88986246	-1.601944663
SLC3A1	5.844265	3.648617695	-1.601775115
CTU1	40.877987	25.52324573	-1.60159832
SLC16A9	50.715064	31.66600838	-1.601561619
PTK7	87.434054	54.63053086	-1.600461373

Supplementary table 4

Gene	Control	miR-1972	Fold change
PRRX2	31.033179	20.1298237	-1.541651806
LIPE	27.30093	17.7096158	-1.541587923
CKLF	64.724861	41.9963165	-1.541203276
CRYGB	8.0428725	5.21900512	-1.541073885
LCE3B	29.609679	19.2188407	-1.540658948
RAB2B	161.0935	104.616979	-1.539840834
SLC12A7	447.34108	290.626443	-1.53923048
REG1A	7.1451142	4.64418826	-1.538506573
LOC101928548	8.2900073	5.39125568	-1.537676525
LINC01490	11.376261	7.39850029	-1.537644259
TAF1A	10.867297	7.0679651	-1.537542528
TRAF1	220.12821	143.178865	-1.53743507
CACNA1C	6.189799	4.02806484	-1.536668165
NUDT13	9.0955856	5.92015973	-1.536375036
SLC23A3	17.222448	11.2129387	-1.53594417
MMP19	14.66931	9.55089844	-1.535908947
S100A3	52.476568	34.1727596	-1.535625692
MIR3144	4.5927344	2.99084378	-1.535598235
FAM83C	6.6598712	4.33728824	-1.535491948
ATP5L2	7.3300679	4.77387197	-1.53545548
ZNF598	129.98172	84.7018812	-1.534578851
ZNF667	37.301925	24.3106227	-1.534387885
HIF1A-AS2	72.609086	47.3239464	-1.534299056
FAM200A	40.320303	26.2830426	-1.5340805
CCDC88B	6.9456125	4.52759516	-1.534062177
SOHLH1	8.1448349	5.30944172	-1.534028498
TNNC1	10.773936	7.02651919	-1.533324761
MIR885	7.1879777	4.69117652	-1.532233476

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
BEGAIN	6.168804	3.94304312	-1.564477948
CD3EAP	149.04319	95.2716548	-1.564402264
TMEM187	45.98227	29.40168852	-1.563932978
TSACC	12.236244	7.828698001	-1.562998659
RNU6-78P	5.227773	3.345450365	-1.562651493
IGLV5-45	4.4866936	2.873032996	-1.561657512
ZSCAN30	33.099794	21.19586268	-1.561615807
MAP2	37.074355	23.74993314	-1.561029861
FRMPD1	5.8554014	3.751331371	-1.560886217
MFSD4	10.80009	6.920317153	-1.560635164
ZRANB3	41.99037	26.94635673	-1.558294904
ALOX5AP	23.134325	14.84791029	-1.55808626
RAB11FIP4	10.051359	6.451456774	-1.557998295
RARRES2	13.769802	8.839238384	-1.557804131
DEFB4B	9.423337	6.049830836	-1.557619917
LCE5A	5.5561869	3.567482143	-1.55745331
LOC100996681	7.5359135	4.840341887	-1.556896942
RDH14	45.46136	29.21419934	-1.556139174
LOC151174	8.2692449	5.315041957	-1.555819301
ARRDC4	50.643078	32.5520058	-1.555759065
PLA2G2F	6.8687358	4.416080424	-1.555391924
SYNDIG1	6.8355775	4.395653645	-1.555076453
MIR27A	32.473905	20.88601319	-1.554815889
RSPH3	49.996413	32.15951122	-1.554638464
SLC22A24	6.3262098	4.072502612	-1.553396124
MIR325HG	14.560617	9.373688292	-1.55334982
MYL5	30.096693	19.38166266	-1.552843718
CEACAM19	69.519363	44.77338626	-1.552693893

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
LINC00640	6.1504502	3.844822666	-1.599670709
RGS7BP	26.909153	16.82973234	-1.598905568
NPNT	10.034536	6.276454825	-1.598758559
CKLF	64.724861	40.49631646	-1.598290071
SNORD114-28	15.607655	9.765434261	-1.598255063
LOC100507065	9.4680539	5.924461899	-1.598128922
BUB1	317.6349	198.7754518	-1.597958402
OR10H2	9.7622519	6.109943127	-1.597764766
KRTAP16-1	7.3870263	4.625081917	-1.597166587
FDPSP2	11.420594	7.152059237	-1.596826017
SLC37A1	238.65705	149.516213	-1.596195118
KCNG4	5.560825	3.48595124	-1.595210194
DHRS4-AS1	94.112613	59.00696257	-1.594940818
LYVE1	114.36157	71.70618858	-1.594863325
AMDHD1	6.6699161	4.183843366	-1.5942079
LOC101927759	14.263708	8.948696638	-1.593942514
LOC101929767	29.364096	18.42730884	-1.593509733
ADAMTSL5	8.7465909	5.488891037	-1.593507845
DMGDH	6.556427	4.114635401	-1.593440575
NFIC	950.95881	597.0064951	-1.5928785
ZER1	125.71699	78.92720136	-1.592822116
MAP3K2	119.61858	75.11051607	-1.592567737
LOC101928658	5.5818446	3.505554995	-1.592285554
TMEM132B	7.5913839	4.767896075	-1.592187368
LINC01476	6.4914345	4.077225284	-1.592120643
LINC01194	12.772876	8.022977653	-1.592036879
ABCG8	7.7969545	4.897657774	-1.591976169
PATL1	759.68258	477.4307636	-1.591188992

Supplementary table 4

Gene	Control	miR-1972	Fold change
TRIM16L	36.684866	23.9430816	-1.532169775
TM4SF1-AS1	7.5655382	4.94004297	-1.531472147
MIR330	12.36471	8.07414008	-1.531396488
LOC101927216	6.3830426	4.16817893	-1.531374433
BCL2L12	58.677852	38.3289551	-1.530901414
PABPC3	7.0355708	4.59587304	-1.530845339
LOC101928360	9.1218145	5.96260956	-1.52983595
LOC101927636	4.1886463	2.73802244	-1.529807159
MIR4502	10.868588	7.10854348	-1.528947317
ADAMTSL5	8.7465909	5.7207572	-1.528921892
TMEM176B	15.360378	10.0468139	-1.528880566
MIR4470	9.0155052	5.89727016	-1.528759064
LOC101929741	5.0268593	3.28866443	-1.528541275
MIR4314	9.3976315	6.15156988	-1.527680199
LINC00515	4.9400682	3.23382803	-1.527622412
OXTR	20.529738	13.4397041	-1.527543886
LOC100506538	6.7682885	4.43085185	-1.527536629
LOC101929261	9.0525054	5.92788929	-1.527104334
LHX1	9.9770347	6.53383296	-1.526980382
LSM14B	102.97938	67.4440667	-1.52688571
LOC101929441	6.103881	3.999185	-1.526281222
KIF27	34.246602	22.4473079	-1.525644048
LOC101928220	12.810443	8.39694327	-1.525607874
SCOC-AS1	7.9276347	5.19671454	-1.525508975
CBR3	47.929402	31.4223976	-1.52532608
CA12	32.345835	21.2064833	-1.525280474
HRH2	6.8454196	4.48953737	-1.524749454
BARX2	6.9224827	4.5404218	-1.524634271

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
SLC20A2	88.264279	56.85150841	-1.552540671
IGLL1	8.8644458	5.710941529	-1.552186402
TRIM45	10.461673	6.742163173	-1.551679027
FAM220BP	21.674971	13.9730048	-1.551203283
CBX4	114.48654	73.84110303	-1.55044463
DDIT4L	50.892764	32.84327187	-1.549564376
LYRM2	48.923857	31.57342849	-1.54952627
ZFP3	52.773315	34.06053916	-1.549397522
BHLHE40-AS1	7.8336264	5.058226864	-1.548690196
NA	9.4541114	6.106909549	-1.548100778
LOC100506098	7.7586796	5.011946539	-1.54803718
PRKCQ-AS1	18.682672	12.0708409	-1.547752319
LOC100507599	14.869213	9.608659771	-1.547480476
MATN1	8.5831027	5.552821968	-1.545719057
TRAV38-1	32.499471	21.02564765	-1.545706052
FCGR3B	6.4286302	4.159795295	-1.545419851
IRX5	6.3455074	4.109945188	-1.543939655
SUDS3	122.25874	79.19240842	-1.543818977
TUBB2B	33.827314	21.91175006	-1.543797919
LCE1E	3.4679067	2.246846486	-1.543455136
RIMS1	7.6402371	4.951236343	-1.543096832
LINC00973	23.066715	14.95560715	-1.542345617
OR11H1	6.3411019	4.112264504	-1.541997587
ZNF488	10.326595	6.700228381	-1.541230297
LOC100505570	13.634208	8.846920247	-1.541124785
SNORD115-15	4.9562122	3.21632184	-1.540956547
CAMK1D	118.00529	76.59833294	-1.540572611
PAG1	9.0811731	5.895683652	-1.54030874

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
ENTPD1	207.00558	130.1274163	-1.590791441
SLC24A3	6.6232422	4.164493446	-1.590407644
MIR4520-2	4.984266	3.134297369	-1.590233923
C1orf86	57.835902	36.40158291	-1.588829304
LOC101929762	10.189832	6.415152739	-1.588400489
ZNF300P1	14.804128	9.320605368	-1.588322568
HSPB9	8.0047751	5.042119701	-1.58758133
ZNF70	99.129903	62.4732715	-1.58675703
GPR124	151.87983	95.72131494	-1.586687635
MCTP2	20.801869	13.11180349	-1.586499419
TRAPPC12	127.79477	80.59144336	-1.585711346
LOC100130872	7.8031601	4.921677933	-1.585467441
GCSH	3.962746	2.49971561	-1.585278739
GNS	1724.4375	1087.873299	-1.585145527
HORMAD2-AS1	8.3896769	5.293703632	-1.584840692
AGFG2	168.82786	106.5477467	-1.584527718
DTWD2	61.323437	38.70686546	-1.584303874
LOC645752	6.6948989	4.225901421	-1.584253452
SPINK6	5.1738845	3.267426359	-1.583473957
MIR4312	16.608596	10.49295655	-1.582832845
TRAV8-6	7.4879175	4.73295601	-1.582080524
PLEKHA8	51.284564	32.42209542	-1.58177822
LINC00690	7.6899102	4.861804973	-1.581698624
ZNF396	6.1963535	3.91808244	-1.581476035
OR2L8	8.7438276	5.530270372	-1.581085021
CDHR3	7.0299389	4.446458214	-1.581019888
AMN1	79.819675	50.48679222	-1.581001116
NA	8.2091373	5.193238318	-1.580735708

Supplementary table 4

Gene	Control	miR-1972	Fold change
ATE1-AS1	32.211449	21.1275888	-1.524615468
WWTR1-AS1	9.338135	6.12508884	-1.524571362
CIB2	39.897261	26.173849	-1.524317681
NA	4.7772744	3.13471606	-1.523989522
ZNF807	5.5599416	3.64879758	-1.523773642
RCSD1	17.906593	11.7549523	-1.523323354
ASB16	19.519411	12.8139203	-1.523297377
LOC728739	12.868266	8.4478453	-1.523260092
LOC101927770	8.1037423	5.32002289	-1.523253269
ZNF627	37.214069	24.4432258	-1.522469638
ZGRF1	29.818801	19.591656	-1.522015361
ATP2A3	17.713774	11.6387654	-1.521963328
SYPL2	9.4971843	6.24039396	-1.521888585
SIRT7	84.303815	55.4018922	-1.521677548
LOC101929762	10.189832	6.69772831	-1.521386249
XAF1	278.50109	183.06632	-1.521312521
ULK1	59.491502	39.108531	-1.521189886
CYP1A2	12.127897	7.97659136	-1.520436004
STARD7-AS1	41.202311	27.101726	-1.520283667
INPP5E	57.305745	37.7180368	-1.519319387
ZNHIT3	119.52279	78.6701549	-1.519290189
SNORA26	46.0822	30.3324374	-1.519238276
SHROOM1	16.591952	10.9213124	-1.519226983
GBP1	306.90235	202.055016	-1.518904876
LOC442028	7.1096508	4.68197249	-1.518516143
OR14A16	5.5492011	3.65488792	-1.518295823
LOXL4	11.52442	7.59114274	-1.518140375
LINC01237	17.647302	11.6246186	-1.518097301

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
BAK1	155.04775	100.6641359	-1.540248189
TMEM147-AS1	16.928648	10.99132447	-1.54018274
MIR4522	15.198889	9.868659863	-1.540116778
BSX	8.8044602	5.716966275	-1.540058103
PPP1R32	23.187463	15.05624255	-1.540056408
RPUSD1	262.60097	170.5271165	-1.53993674
GPT2	65.360302	42.45304111	-1.539590565
KRTAP6-3	12.028831	7.813135229	-1.539565245
IGLV2-18	8.936589	5.805722521	-1.539272504
IRF1	306.79781	199.3567099	-1.538938978
RPL39L	83.371316	54.17662964	-1.538879716
C17orf105	7.1301746	4.634707492	-1.53843033
PAQR8	26.804659	17.42856036	-1.537973217
ZNF333	40.837832	26.56448061	-1.537309651
DTHD1	5.0838874	3.308986004	-1.536388316
ZNF823	57.600836	37.49713938	-1.536139483
HAPLN1	132.11544	86.02491972	-1.535781
HIST1H2BC	18.051874	11.75548841	-1.535612378
PPP1R14D	6.6276733	4.31632733	-1.535489042
PP13	16.169077	10.53094051	-1.535387752
SLC24A3	6.6232422	4.314683806	-1.535046949
ZNF334	11.72788	7.640247424	-1.535013093
ZFP14	10.7578	7.011419219	-1.534325627
HHATL	6.6406516	4.329513687	-1.53381004
TGFB3	18.726271	12.20915219	-1.533789616
LOC93463	7.9878425	5.208515438	-1.53361213
GADD45B	274.90903	179.2662254	-1.533523824
ADAM28	8.4714608	5.5254026	-1.533184346

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
ATP9B	74.457518	47.1088731	-1.580541278
CYP2A7	31.482246	19.9228418	-1.580208607
CTNNA3	7.4650716	4.728502346	-1.578739104
PHF19	213.91526	135.5230446	-1.578441973
SRGAP2	356.41246	225.8815353	-1.577873391
LOC101928162	13.777018	8.733412483	-1.577506824
PNMAL2	10.589205	6.71275819	-1.577474589
LOC101928800	5.2658414	3.33868707	-1.577219217
HCRTR1	15.346346	9.73003696	-1.57721354
ZNF660	6.8051503	4.314996393	-1.577092929
MGC72080	81.176003	51.47818327	-1.576901077
SLC32A1	13.883544	8.807619539	-1.576310555
HIST1H2AK	53.125797	33.71174284	-1.575884035
VIPR1	24.411765	15.49310713	-1.575653307
ATMIN	598.76379	380.0312165	-1.575564741
POTEF	4.7549989	3.018000803	-1.575545949
EXTL1	7.0685368	4.488577241	-1.574783367
LOC100129046	8.918356	5.668543867	-1.573306347
ZNF248	17.83672	11.34402043	-1.572345556
TMBIM4	413.07806	262.7286003	-1.5722615
GBAP1	26.174715	16.65030014	-1.572026607
MCHR2-AS1	8.9811667	5.714976639	-1.571514162
MDFIC	46.56503	29.64331029	-1.570844469
FAM43A	564.38897	359.2924479	-1.570834487
C14orf1	569.26501	362.4846974	-1.570452518
KIF4A	278.72559	177.653583	-1.568927498
FAHD2CP	36.300657	23.13935465	-1.56878432
PF4V1	7.6001207	4.848588622	-1.567491351

Supplementary table 4

Gene	Control	miR-1972	Fold change
LINC00883	36.448005	24.0117037	-1.51792665
USP29	5.6542535	3.72610891	-1.517468654
BRE-AS1	9.0230632	5.94613498	-1.517466928
MIR4748	31.311802	20.6368556	-1.517275798
CSAD	34.141008	22.5097402	-1.516721556
PRKCQ-AS1	18.682672	12.3223095	-1.516166426
MAFG-AS1	27.287296	18.009793	-1.515136567
MEG8	31.040073	20.4920997	-1.514733666
IGLV10-54	22.41892	14.8025112	-1.51453494
LINC00592	7.1353437	4.71619305	-1.512945647
RPL34	261.86508	173.158682	-1.512283869
LOC101928461	8.8181096	5.83280258	-1.511813488
RWDD2B	96.594744	63.9330787	-1.51087272
ATP6V0A4	10.626668	7.03581653	-1.510367354
CDSN	8.0148512	5.30677612	-1.51030513
LOC101928737	10.097695	6.6862404	-1.510220209
SPATA31A6	9.0196907	5.97301374	-1.510073653
TMEM170A	134.83287	89.2989916	-1.509903605
OR8A1	9.1542338	6.06344078	-1.509742422
ZFP36	97.860872	64.820353	-1.50972445
SOGA3	9.2232002	6.10996852	-1.509533172
SLC24A3	6.6232422	4.38769941	-1.50950227
LOC101927837	7.4135184	4.9133421	-1.508854516
ZNF257	9.2639583	6.14004636	-1.508776596
OR10G4	5.8896489	3.90397219	-1.508629826
MTO1	157.63559	104.499732	-1.508478454
MIR655	4.0717376	2.6994844	-1.508338995
SLC25A51	88.171316	58.462045	-1.508180491

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
AQP4-AS1	5.8767973	3.834315542	-1.532684838
PRAMEF7	13.846143	9.03596659	-1.532336709
LOC93622	41.398129	27.0406604	-1.530958495
SNORD116-13	7.0645466	4.615788212	-1.530517917
NARFL	80.232998	52.43617233	-1.530107836
VEGFA	99.577118	65.10426735	-1.529502166
LOC339622	5.1025726	3.336161245	-1.529474209
AKAP7	20.886218	13.65590133	-1.529464646
AJUBA	94.311506	61.66776057	-1.529348648
UPF3A	137.7567	90.07772038	-1.529309405
GPR133	9.6862989	6.336684385	-1.528606803
TMEM116	22.50551	14.72290823	-1.52860493
DCAF8L1	4.9233919	3.221850497	-1.528125505
ADAMTS9-AS2	9.306212	6.091238835	-1.527802837
SCIMP	7.4080464	4.850728751	-1.527202781
CYTH3	37.03605	24.25111888	-1.527189312
PLEKHA8	51.284564	33.58438808	-1.527035843
RPE	30.732179	20.14333326	-1.52567497
LOC100132731	10.057052	6.592383155	-1.525556363
TTC32	14.021298	9.197568103	-1.524457061
CXCL16	101.05723	66.30569944	-1.524110825
NAT9	175.84494	115.3889649	-1.523932071
MIR4532	8.2429232	5.410513013	-1.523501219
SLC35G1	18.492569	12.14441666	-1.522721872
SLC22A31	14.002733	9.197952578	-1.522374997
TRAJ28	10.590994	6.958285713	-1.522069442
STC2	390.75803	256.7444725	-1.521972522
TRPM2-AS	13.169877	8.65680481	-1.52133227

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
PACSIN1	10.04335	6.407528199	-1.567429722
RETNLB	7.3809216	4.709088251	-1.567378054
SOGA3	9.2232002	5.885416332	-1.567127904
IPO5P1	24.559373	15.67439641	-1.566846484
ZNF14	13.135545	8.383626504	-1.566809367
LINC00702	36.317201	23.18108077	-1.566674194
VEGFA	99.577118	63.56144174	-1.566627742
PYHIN1	5.8114473	3.710005044	-1.566425703
SPATA6	42.621934	27.21135222	-1.566329139
ERP27	18.815325	12.01365714	-1.566161341
MCTP1	577.13372	368.5241464	-1.566067585
BOLA1	37.29838	23.82170848	-1.565730687
IFI27L1	63.499362	40.56120334	-1.565519668
ECM1	63.869389	40.80051336	-1.565406512
C10orf54	19.827085	12.6662543	-1.565347161
KIF18B	90.288157	57.69631723	-1.56488596
MRAP2	23.924328	15.28878175	-1.564828902
LOC643072	61.058149	39.01943534	-1.564813759
ARRB1	760.59495	486.1447416	-1.564544234
LOXL4	11.52442	7.366210411	-1.564497841
COL4A6	9.1911727	5.875927174	-1.564208073
MTMR9LP	17.80459	11.38250515	-1.564206648
C16orf86	5.5596866	3.55503349	-1.563891473
LY86	7.1508531	4.572479973	-1.56388943
NKAIN4	8.1549654	5.214552518	-1.563885947
WASH3P	36.421316	23.29341532	-1.563588474
LXN	152.76321	97.72632071	-1.563173618
TACC1	1070.4212	685.131529	-1.562358741

Supplementary table 4

Gene	Control	miR-1972	Fold change
TOB2P1	18.19535	12.0676212	-1.507782648
RFPL2	10.748326	7.12934504	-1.507617528
LOC101928859	10.40721	6.90359969	-1.507504886
LOC100287175	17.252808	11.4450469	-1.50744758
CD3EAP	149.04319	98.8995238	-1.50701628
DNAJA4	119.82076	79.5091311	-1.507006237
XRCC3	54.854267	36.4070924	-1.506691778
PINLYP	10.108154	6.71024396	-1.506376568
XKR6	25.032055	16.6186905	-1.506259146
KIF21B	20.903314	13.8783524	-1.506181242
RPS15AP10	11.545018	7.66654895	-1.505894975
WBP11P1	7.8084095	5.18595581	-1.505683762
CCDC85C	29.398273	19.527281	-1.505497508
GUCY2EP	9.9348274	6.5996235	-1.505362757
DANCR	631.39087	419.472399	-1.505202414
DHX58	18.842387	12.5183698	-1.505179001
UNC5D	6.4648681	4.29667438	-1.504621362
TRBV5-7	7.0332472	4.6759843	-1.504121227
P2RX6P	6.0267449	4.00702547	-1.504044569
SNORA44	69.617713	46.3213172	-1.50293033
LINC01208	6.4286302	4.27932679	-1.502252699
HES7	13.320368	8.86707082	-1.502228637
APOL6	58.967745	39.2536503	-1.502223231
KIF1A	38.73679	25.7872337	-1.50216926
EHHADH-AS1	7.6156899	5.06997248	-1.502116605
MIR3657	8.1914568	5.45337177	-1.502090301
NOX5	9.0679554	6.03751011	-1.501936271
LOC101929380	12.992967	8.65765878	-1.500748323

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
OSBPL6	35.895585	23.60269804	-1.520825515
DNAJB9	59.493049	39.12176156	-1.520714995
APOL6	58.967745	38.78209683	-1.52048884
FAM184A	23.698537	15.58952086	-1.52015816
ZNF627	37.214069	24.49032	-1.519541969
LOC101928947	5.459051	3.593780923	-1.519027194
TMSB4Y	6.4359201	4.237751353	-1.518711119
ZNF671	21.946761	14.45934154	-1.517825742
FAM86HP	34.509355	22.73750858	-1.517728061
AGMAT	16.41605	10.81750839	-1.517544458
LOC254896	51.921316	34.22206536	-1.517188257
FAM19A5	12.576935	8.290007295	-1.517119847
HDAC10	62.26814	41.04959857	-1.516900105
KLRC4	7.2162493	4.757493376	-1.516817521
C19orf38	9.6608318	6.371289029	-1.516307255
C1RL-AS1	11.418282	7.534999491	-1.515365998
SNORD116-26	24.756867	16.34668094	-1.514488928
RASGRF2	88.511718	58.44985635	-1.514318834
DSCR10	9.1352676	6.033531184	-1.514083108
FAM195A	29.503512	19.48919708	-1.513839267
MIR874	5.983161	3.953410627	-1.513417543
IFI44	133.41588	88.16262847	-1.513292876
MIR222	30.777858	20.34765121	-1.51260006
ALDH1A3	81.157277	53.66469868	-1.512302849
SNORD12B	238.29891	157.622235	-1.511835615
MDGA1	18.568745	12.28303262	-1.511739491
ALDH1L1-AS2	8.6840477	5.746559034	-1.511173503
LOC101926901	10.828049	7.165697354	-1.511094916

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
NBEAL2	137.79518	88.23371317	-1.561706655
SLC52A2	257.38075	164.8743714	-1.561071914
NA	29.788762	19.08278512	-1.561028022
RNU105B	8.2712818	5.299101283	-1.560883882
LOC101927617	5.077336	3.254265263	-1.560209634
HAPLN2	8.8312478	5.661242886	-1.55994858
MIR320D2	4.8950297	3.138538023	-1.559652836
LOC283683	5.9040635	3.786009139	-1.559442473
DBF4B	37.531115	24.06951893	-1.559279819
CCDC106	34.198748	21.93703971	-1.558949987
FAM200A	40.320303	25.86914457	-1.558625294
TACC3	220.69691	141.6579654	-1.557956247
REG3G	7.9164914	5.081690715	-1.557845965
ZNF558	24.188611	15.52818994	-1.557722529
SCN4B	11.730127	7.530926786	-1.557594124
PTPRG-AS1	5.6170118	3.60700539	-1.557250735
ASRGL1	132.63008	85.23668467	-1.556021106
MIR3944	23.828224	15.31824208	-1.555545609
LOC101927751	38.62771	24.84038323	-1.555036804
LRRK2	6.3593877	4.089709164	-1.554973099
SOCS3	104.60162	67.27272788	-1.554888932
CLEC17A	7.0649879	4.546480421	-1.553946629
PPP1R3G	9.9707953	6.417524656	-1.553682423
IGF2	11.065759	7.123953725	-1.553317098
LOC101929261	9.0525054	5.830522171	-1.552606296
MARVELD1	217.01257	139.8254935	-1.552024349
CRYBB2P1	87.836309	56.59824962	-1.551926248
DLEU2	18.909318	12.1850353	-1.551847609

Supplementary table 4

Gene	Control	miR-1972	Fold change
LINC00671	14.051091	9.36332442	-1.500651922
USP17L10	18.66616	12.4394186	-1.500565298
DPF1	20.484293	13.6524459	-1.500411983
NSUN5	71.939982	47.9497415	-1.500320531
NCR3LG1	172.78962	115.169319	-1.500309476

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
DENND2C	9.6779938	6.406985849	-1.510537726
HIST1H2BE	22.4107	14.83720899	-1.510439064
SEMA4B	60.021762	39.73937041	-1.510385319
OR56B4	9.7229856	6.439835055	-1.509819045
CST8	6.2747927	4.158653129	-1.508852156
FAT1	65.031288	43.13926209	-1.507473359
SNHG20	42.503124	28.201604	-1.50711724
TRBV5-7	7.0332472	4.667080983	-1.506990615
CFAP44	10.499763	6.96945111	-1.50654086
ZNF585A	36.317585	24.11446719	-1.506049673
LUC7L2	97.361092	64.65016497	-1.505968187
PGAM1	16.892125	11.21704009	-1.505934264
FCN2	7.0788299	4.70072915	-1.505900408
LOC101928239	8.4620651	5.619908352	-1.505730092
FAM92A1P2	6.4670072	4.295001541	-1.505705435
BAG2	61.856752	41.08494088	-1.505582108
BREA2	9.0489016	6.010561146	-1.505500296
NOX5	9.0679554	6.024036759	-1.505295499
CDR2L	166.12077	110.3927503	-1.504815932
PDF	95.571317	63.5463157	-1.503963151
LINC00398	8.4715304	5.633267247	-1.5038396
PPBPP2	5.7475875	3.823603337	-1.503186126
CA13	72.115779	47.98766391	-1.502798277
CLCNKB	6.3613243	4.233704236	-1.502543388
MIB2	39.356409	26.19767884	-1.502286115
FSTL3	95.728978	63.72990257	-1.502104564
PINLYP	10.108154	6.730003967	-1.501953686
EYA4	6.2626233	4.170974237	-1.501477348

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
C3orf35	19.468547	12.54782078	-1.551548066
KRTAP19-3	5.6738898	3.657207118	-1.551426994
PCAT7	10.352334	6.673153082	-1.551340669
LOC101927372	5.658053	3.64745694	-1.551232301
SNORD91A	16.108199	10.38460263	-1.5511618
LOC101927886	46.293567	29.85020777	-1.550862458
C17orf105	7.1301746	4.600217483	-1.549964671
PDGFRL	179.43865	115.7897069	-1.549694332
RPE	30.732179	19.83409889	-1.54946184
ZNF182	43.991376	28.39800369	-1.549100997
LPAR4	34.699389	22.40769831	-1.548547677
LOC284344	8.4920666	5.485807739	-1.548006607
MIR4674HG	17.479948	11.29409325	-1.547707049
ACKR3	324.43656	209.6450947	-1.547551411
SLIT3	93.920064	60.70487232	-1.547158583
LINC00276	6.0537091	3.913478067	-1.546887194
LINC00226	9.0623846	5.858711874	-1.54682203
LOC101926893	8.6738539	5.608472671	-1.546562561
LRIG3	409.88836	265.0646316	-1.546371363
SMR3A	4.9354038	3.191795103	-1.546278395
CHST7	42.901494	27.74921832	-1.546043332
ZNF503-AS2	8.8183893	5.703918953	-1.546022895
TMEM242	173.57581	112.2829213	-1.545878965
CATSPER2P1	13.060394	8.448930192	-1.54580442
UTS2	6.8898436	4.457208025	-1.545775644
ITGB4	27.704181	17.92686242	-1.545400431
CBX7	21.728446	14.06131429	-1.545264263
ZNF337	49.469843	32.01683811	-1.545119576

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change
SH3RF1	258.91782	172.4839248	-1.501112739
SDHAF1	29.672038	19.76969005	-1.500885342
LOC101928809	6.8479926	4.562789365	-1.500834698
GCNT4	9.2819481	6.184524111	-1.500834661
CNIH2	8.545971	5.695106558	-1.500581414

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
C6orf195	6.7948175	4.397602776	-1.545118531
RPL23A	480.72805	311.1741691	-1.544884184
NA	4.7772744	3.092783164	-1.544652234
HOXA6	65.782768	42.60933752	-1.543858025
TBC1D26	13.75616	8.910534465	-1.543808603
ZNF30	24.107179	15.61855402	-1.543496214
ATOH8	58.220523	37.72412509	-1.543323336
GAGE12J	8.4077755	5.447994519	-1.543278995
SIGLEC7	6.4465555	4.177737365	-1.543073427
LOC101928026	5.6446309	3.658334901	-1.542950849
CRYAA	12.109796	7.850389201	-1.542572686
SGIP1	119.65641	77.6147916	-1.541670123
SNORA74A	28.062581	18.20354205	-1.541600057
NA	8.6392683	5.606746209	-1.540870235
CPXM1	26.17139	16.98558012	-1.540800477
TRAV12-1	8.7949952	5.709002289	-1.540548543
LPHN3-AS1	7.1244157	4.625027581	-1.54040503
LOC101927391	4.895287	3.177986958	-1.540373533
KCTD12	533.39504	346.4170618	-1.539748188
TMOD1	55.14979	35.8249017	-1.539426126
MYH13	6.2869968	4.086449893	-1.538498435
CCDC115	71.020973	46.16953553	-1.538264842
LOC101928794	14.206231	9.235904267	-1.53815266
LMNTD2	18.279897	11.88577127	-1.53796473
CGNL1	219.60331	142.7892236	-1.537954363
LOC653786	5.6338239	3.663198644	-1.537952053
SNORD114-9	14.247744	9.265479559	-1.537723281
GMPR	160.75197	104.5489042	-1.537576762

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
TTC30A	54.644541	35.54585743	-1.537297042
GPR146	18.76388	12.20734965	-1.537096959
CEACAM1	104.53817	68.04031513	-1.536415161
NCAM1-AS1	8.2587365	5.376714647	-1.536019117
HOXC10	9.5553368	6.221147349	-1.535944456
PRSS27	10.767736	7.011725723	-1.535675652
IGFBP6	12.201261	7.945467833	-1.535625206
IGKV1-8	5.6086441	3.652510342	-1.535558727
LOC100506538	6.7682885	4.409255638	-1.53501839
B3GNT1	54.699955	35.64770271	-1.534459461
GTSF1	12.747757	8.308378354	-1.534325509
NDUFAF5	59.917823	39.05286602	-1.534274667
KDELR3	302.1096	196.9213157	-1.534164024
ZNF513	119.54124	77.93780902	-1.533802897
TGFB3	18.726271	12.20915219	-1.533789616
MYOM1	6.774186	4.420851941	-1.532325917
MMP28	9.9739543	6.509820985	-1.53213957
TREX2	9.5569505	6.237927041	-1.532071541
TSPAN15	389.70511	254.3794715	-1.53198333
PIK3C2A	687.30851	448.7220496	-1.531702109
SNORA79	15.12281	9.879661352	-1.530701288
KIAA0930	482.93253	315.5290271	-1.530548676
BRWD3	143.33386	93.65485092	-1.530447816
MIR3667	19.230177	12.56507551	-1.530446632
ZNF572	6.7783237	4.430252841	-1.530008326
COL3A1	57.227029	37.4053716	-1.529914732
ZNF568	21.05087	13.75955959	-1.52990872
SLC25A51	88.171316	57.63395017	-1.529850296

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
SPSB4	6.4707897	4.229727004	-1.529836252
LOC101928201	5.1035457	3.337754942	-1.529035475
FAM114A1	746.67304	488.371062	-1.52890516
LOC101928248	7.1639156	4.685682129	-1.528894916
RBCK1	301.87331	197.5130237	-1.528371682
HS3ST1	32.231698	21.0933594	-1.528049525
TRBV11-2	4.3946466	2.876794259	-1.527619346
OCM	6.2032138	4.061116721	-1.527465036
SKP1P2	5.3633781	3.511390197	-1.527422997
KRT14	6.480772	4.243373431	-1.527268825
DLX5	7.6189546	4.989084214	-1.527124867
FGD6	111.9254	73.29224538	-1.527111139
TBX6	9.9385975	6.509880035	-1.52669442
RASAL1	11.075094	7.25627082	-1.526279003
LOC646522	8.19025	5.367213085	-1.525978165
MIR9-1	13.776751	9.029386229	-1.525768294
KRTAP10-5	6.1442765	4.027336747	-1.525642587
PKD1L2	7.2693816	4.764924636	-1.525602643
CACNA1C	6.189799	4.058544224	-1.525127894
ADAM7	5.8441928	3.832931698	-1.524731787
LOC283693	7.8214227	5.132969498	-1.523761772
NDUFA5	12.261111	8.048102777	-1.523478397
LOC101929412	8.1744295	5.366415513	-1.523256899
GOLGA1	113.57277	74.56829074	-1.523070622
NA	11.137455	7.313569269	-1.522848113
SLC27A3	68.991621	45.32375397	-1.52219565
LOC730101	11.686308	7.680899802	-1.521476376
MIR377	10.419383	6.848217397	-1.521473789

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
FLJ37505	7.4090032	4.870494397	-1.52120147
CTGLF12P	128.61244	84.5608541	-1.520945419
FUK	23.044978	15.15285165	-1.520834369
KAT6A	337.22008	221.7667986	-1.520606686
RNU6-57P	7.0835444	4.658601084	-1.520530372
OR2T35	10.087852	6.63652202	-1.520050935
ZFAT-AS1	7.8062756	5.136330722	-1.519815611
RGS21	5.3269622	3.505664357	-1.519530018
S100A3	52.476568	34.53896804	-1.519343821
NUDT13	9.0955856	5.989220257	-1.518659397
C2orf69	70.792144	46.62717371	-1.518259387
SELP	66.8662	44.04197655	-1.518237953
HRH2	6.8454196	4.514309561	-1.516382418
TRAJ58	5.6882874	3.751847212	-1.516129801
ACKR4	8.9036246	5.873757886	-1.515831047
LINC00314	7.2696764	4.796647408	-1.515574472
CCL7	9.0266805	5.958414078	-1.514946823
ARHGEF3	83.930842	55.40219549	-1.514937104
MEGF8	45.437363	29.99682215	-1.514739222
MKI67	792.22702	523.1463027	-1.514350803
BLACAT1	4.9279266	3.254265263	-1.514297754
EMB	6.5369248	4.317062198	-1.514206759
TRAJ61	5.7347238	3.788893097	-1.513561797
HMSD	8.04396	5.314881969	-1.513478578
HPR	4.5867579	3.031045825	-1.513259183
PCDH10	620.84701	410.4937684	-1.512439553
LRRC23	13.604741	8.9966914	-1.512193825
TTTY22	8.1246469	5.373366105	-1.512021835

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
HIST1H3G	201.42277	133.2170507	-1.511989427
SDCBP2-AS1	14.140548	9.356700506	-1.511275051
HIST1H4A	42.93981	28.41757112	-1.511030248
SEMA4G	25.595941	16.94202031	-1.510796244
CGB8	13.07791	8.65680481	-1.510708606
KBTBD6	64.181428	42.48938209	-1.510528618
SESN3	110.95623	73.46139498	-1.510401843
OR2T11	5.730977	3.795296176	-1.510021027
RABL6	131.02082	86.77147018	-1.50995279
DSCR10	9.1352676	6.050329715	-1.509879308
GBP4	300.15886	198.8413493	-1.509539431
FNBP1	307.30962	203.6978243	-1.508654402
CA12	32.345835	21.4409369	-1.508601751
RERE	399.78838	265.0341074	-1.508441246
RNF43	7.0761979	4.691339735	-1.508353323
GNAS-AS1	6.7462124	4.472649551	-1.508325733
ADAM30	6.9067487	4.579418115	-1.508215355
TCF15	13.881516	9.205393159	-1.507976443
LOC100129215	14.215139	9.426852167	-1.507941192
FLJ13224	19.363927	12.84240297	-1.507811837
LOC101927752	195.94617	129.9595123	-1.507747799
TNS1	98.561735	65.37393838	-1.50766096
OR7A10	6.829997	4.531188684	-1.507330074
UACA	525.69806	348.799884	-1.507162371
F13A1	5.2262498	3.467915706	-1.507029087
FCGR2A	7.3911952	4.904968211	-1.506879335
TMEM42	34.046316	22.59793315	-1.506611935
LOC101927274	6.2801999	4.168535815	-1.506572127

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
CSRP2BP	17.688123	11.74159113	-1.506450268
C10orf71	7.8683602	5.223124947	-1.506446868
GUSBP2	7.7402178	5.138412124	-1.506344293
MIR4691	17.690165	11.74413972	-1.50629725
CPQ	108.37397	71.96455764	-1.505935335
DIO1	6.7677849	4.494201963	-1.505892468
GPHB5	7.4172668	4.928285408	-1.505040035
VCX2	24.73997	16.44069287	-1.50480092
OR2F1	8.6910449	5.777607731	-1.504263587
LOC101927560	4.9278377	3.276016291	-1.504216485
LOC100287175	17.252808	11.47324852	-1.503742225
LOC101927282	5.6502401	3.75829847	-1.503403778
CHI3L1	6.5078584	4.329708451	-1.503070818
NR2F2-AS1	18.231533	12.12971011	-1.503047675
SRD5A1P1	5.112533	3.401722237	-1.502924895
LOC101928472	14.193275	9.444593434	-1.502793646
CRHR1-IT1	20.089424	13.36924399	-1.502659691
LOC101928909	6.1564692	4.097400698	-1.502530417
DENND1C	9.5676557	6.369402923	-1.50212756
LOC101929484	11.232121	7.47793725	-1.502034677
TMCO5A	6.1617217	4.102585859	-1.501911704
SPIN2B	122.95207	81.87131646	-1.501772212
SSH3	82.278096	54.79717961	-1.501502382
FOXD4L3	74.310829	49.49631646	-1.501340596
DIAPH3-AS1	11.643144	7.755515301	-1.501272793
SH2D6	13.544248	9.023036654	-1.501074269
BTBD17	10.717407	7.141742486	-1.50067121
MIR433	6.323033	4.214097458	-1.50044773

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change

Supplementary table 3

Gene	Control	miR-574-5p	Fold change
NEUROG2	7.2685342	4.844325675	-1.500422291
RSPO1	10.472297	6.980557448	-1.500209266
LINC00202-2	5.6801387	3.786562555	-1.500077867

Supplementary table 4

Gene	Control	miR-1972	Fold change

Supplementary table 5

Gene	Control	miR-4792-3p	Fold change